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# PELLAGRA

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DR. A. MARIE

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TRANSLATED BY  
HUG. LAVISSE AND BABU



Adrian Beuvers















EGYPTIAN PELLAGRA.  
Courtesy of Dr. F. M. Sandwith.

# PELLAGRA

BY

*mand*  
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With Additions, Illustrations, Bibliography and Appendices

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## TRANSLATORS' PREFACE

We feel that we need plead no excuse at this time for offering the American profession a monograph on pellagra. The recent recognition of the prevalence of this serious disease in the United States, its importance as a public health problem, and the absence of an English treatise upon a subject so vital, seem to us ample justification of this effort on our part.

With a full comprehension of the comparatively limited experience of ourselves and of all American students of this disease, we have deemed it advisable to offer a translation, rather than attempt an original work. We selected, for such translation, Dr. A. Marie's "*La Pellagre*," Paris, 1908, for the reasons that it is recent; that it seemed the most suitable work, both in subject-matter and in size; that it would lend itself more readily to the adaptation necessary for the needs of the American physician, and, above all, that it is largely an abridgment of Professor Lombroso's important work—*Trattato Profilattico e Clinico della Pellagra*, Turin, 1892—itsself too extensive for translation, yet without which no present treatise on the malady could be considered complete.

For his generous permission thus to adapt his book to our purposes and for many other courtesies, we herewith record our profound gratitude to Professor Marie.

Having been prepared for readers long familiar with the subject, and being, as it is, not only a trans-

lation, but likewise an abridgment of Professor Lombroso's treatise, Doctor Marie's book presented many points too succinctly for American students. Moreover, there are in the original French work omissions of some features which we have thought necessary to supply in the present translation. This has required in many places rather extensive additions,—liberties to which Doctor Marie has very graciously consented. Such additions are shown by the conventional use of brackets [     ].

We have earnestly striven to deal adequately with all these difficulties, and in so doing have not only consulted a great many original sources, but we have, for the sake of clearness, practically compared, word for word, the French text with the original Italian of Professor Lombroso. We have also endeavored to include the latest opinions regarding the possible parasitic origin of pellagra.

Certain striking phases of the history of the subject which could not be included in the body of the book, have been inserted as appendices.

We have compiled an English bibliography upon pellagra and have, in addition, listed many of the most important foreign contributions to the subject. Our obligations to the literature of pellagra are hereby acknowledged.

For the privilege of using certain data and photographs we are especially indebted to Surgeon-General Walter Wyman, U. S. Public Health and Marine-Hospital Service, who with prompt comprehension of the importance of pellagra in this country, has in many ways stimulated investigations upon this new problem.

For permission to use photographs illustrating types of pellagra occurring in different countries and for other favors, we are indebted to Dr. F. M. Sandwith and Dr. L. W. Sambon, London, England; Dr. John Warnock and Dr. R. G. White, Abbassia, Cairo, Egypt; the late W. Bayard Cutting, Jr., of New York, and formerly U. S. Vice-Consul, Milan, Italy; Dr. George A. Zeller, Peoria, Ill., and Dr. J. J. Watson, Columbia, S. C.

In addition to his friendly interest in our work we owe a further debt of gratitude to Professor Lombroso for a special preface to this translation, which was received only a short time before his lamented death. To G. W. Manly, Ph. D., of Columbia, S. C., we are under many obligations for assistance in the translation, in preparing manuscript and in seeing the book through the press.

To the publishers we are thankful not only for their unsolicited interest in assuming the responsibility for the book, but also for their great forbearance and patience at unavoidable delays.

Finally, while recognizing its shortcomings we earnestly hope that this little book may prove helpful and stimulating both to the clinician and the sanitarian in dealing with this important disease.

THE TRANSLATORS.

Columbia, S. C., October 1, 1910.



## PREFACE

BY PROFESSOR C. LOMBROSO.

It is impossible to estimate at once the harm which has resulted from the many visionary and obscure theories that have been advanced regarding the etiology of pellagra.

Had it been a question of purely theoretic import, nothing would have been lost but time and paper and perhaps a little of the reputation of those authorities who have too often been misled by their chimerical plans of salvation. But in combating pellagra great sums of money have been misspent through the failure to attack the true causative factors.

The most diverse and untenable hypotheses have been considered in turn. In former times the sun, impure water, insanitary dwellings and even the absence of salt were regarded as the real causes. The expense incurred on the basis of these Quixotic presumptions has been much greater than it would have been to attack, at the root, the actual causes of the malady. The deception which followed all these vain attempts not only retarded but even thwarted serious and effective investigation.

If obstinate antagonism to my theory of pellagra has checked, for a time, my scientific career, it has at least led to a definite orientation of the research work in that direction where I was engaged; whereas, otherwise, the blind and ineffective gropings would have been continued. A phalanx of skillful and talented investigators has undertaken



the experimental study of the etiology; others have attacked the statistical and agricultural side of the question; by profound researches eminent pathologists have thrown light upon the morbid anatomy; therapeutic and hygienic investigations have been extensively carried on; in short, continued opposition has impelled me to struggle with the greatest energy in order to perfect my clinical knowledge and my experimental methods. Furthermore, I have by a series of bold, but encouraging experiments, tested the application of my theory by the therapeutics of cutaneous diseases, and thus, the theory held by me about pellagra has found in a reciprocal way (*a posteriori*) its confirmation.

Finally, I have sustained as paramount preventive measures against pellagra: the drying of Indian corn and the exclusion of the spoiled grain.

Since these methods have been employed upon a large scale our hopes have been fully realized; the number of fatal cases of pellagra—the only source of statistics which merits confidence—has shown in consequence a proportionate reduction. Such a result is, indeed, well worth the personal sacrifices of an investigator.

Dr. A. Marie has been desirous of giving in a small volume a complete résumé of my work and of the actual state of the pellagra question.\*

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\*Lombroso, C.—*Studi clinici ed esperimentali sulla natura, causa e terapia della pellagra*. Bologna, 1872.

\*I veleni del mais e la loro applicazione all' igiene ed alla terapia. Bologna, 1878.

\*Trattato profilattico e clinico della pellagra. Turin, 1892.

\*Lombroso and Ottolenghi.—*L'azione tossica dell' *oidium lactis* nella polenta*. 1890.

He has my gratitude for his efforts, and it is my wish that this work may make our investigations and their happy results better known in France. It is likewise my wish that it may facilitate and encourage the task of all who have undertaken to struggle for the liberation of our race from the social poisons which lie in wait under the cover of ignorance, selfishness and poverty.

*Turin, Italy.*




## PREFATORY NOTE TO THE TRANSLATORS.

I wish duly to comply with your request for a brief prelude to the English translation of Doctor Marie's compilation of my work by announcing the more recent observations made this year, in my laboratory, upon the cause and prophylaxis of pellagra.

First of all, from the experiments made by Professor von Deckenbach of St. Petersburg, the conclusion has been reached that the culture of *oöspora verticilloides* from corn, produces phenomena in animals similar to those of pellagra, as was to be anticipated, since in Bessarabia when corn is much affected with *oöspora*, pellagra is likely to be prevalent.

Many scientific inquiries are still raised as to the possibility that pellagra may originate even from sound corn. With Doctor Audenino, I carried out a series of experiments upon animals with the result, to be sure, that rabbits fed on sound corn died after a certain time, but I satisfied myself that our results demonstrated the fact that we were dealing, not with a poison derived from corn, but with the impossibility of adapting the food used, a grain, to the natural requirements of herbivorous animals. This is emphatically proven because feeding with corn, but, at the same time, with an abundance of greens also, does not cause death in rabbits; and since pigeons and chickens, granivorous creatures, can be fed on such corn alone without harm.



Finally, I have shown that *penicillium* and *aspergilli* of corn are truly pellagrogenous but only when growing upon spoiled corn, from which they imbibe toxic substances; while, on the contrary, when growing upon other plants or material, which have not undergone putrefactive change, they are absolutely harmless.

In conclusion, having observed how one of the causes of pellagra arises from the fraudulent methods of millers, we have introduced with great advantage in pellagra-stricken districts a rapid hand-mill (Bamford) which furnishes fresh meal, in the necessary quantities for daily use, without recourse to the lethal products of the wholesale dealers. Here, again, sound Indian corn scores a point. This method, I believe, is worthy of trial and adoption in America.

C. LOMBROSO,

Professor of Clinical Psychiatry.

Turin, Sept., 1909.

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## CHAPTER I

### HISTORY AND GEOGRAPHY OF PELLAGRA.—RELATION OF THE DISEASE TO CORN.

"If you should traverse the hills of Brianza and Canavese you would most likely meet some pitiable wrecks of humanity, with eyes fixed and glassy, with pale and sallow faces and arms fissured and scarred as by a burn or large wound. You would see them advancing with trembling head and staggering gait like persons intoxicated or, indeed, as though impelled by an invisible force, now falling on one side, now getting up and running in a straight line like a dog after its quarry and now again falling and uttering a senseless laugh or a sob which pierces the heart—such are the pellagrins, poisoned by the toxins of spoiled Indian corn." [With this word picture Lombroso begins his latest and most elaborate treatise on pellagra.]\*

Food adulterations belong to all times and fraudulent methods have been applied to every substance capable of nourishing human beings. It is not alone the intrinsic value of the materials which induces adulteration, but also their extensive consumption; hence, cereals produced in considerable quantities are often, in the course of varied handling, subject to sophistication for the purpose of hiding their defects. Indian corn is one of the cereals very frequently adulterated because in many countries its products are in general use as food.

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\**Trattato proflattico e clinico della pellagra, Turin, 1892.*



Alterations in corn are the cause of pellagra. The occurrence of this disease presupposes the general use of corn as food. That is to say, the geographical distribution of pellagra corresponds to the zone in which corn is cultivated and in common use as food. But to cause pellagra it is not sufficient merely to use corn; it is further necessary that the corn so used should be spoiled. The important question, however, is, what among the divers changes to which this grain is susceptible, are the special ones we should incriminate as producing pellagra?

After a short historical glance at the problem in a general way, we shall proceed to the examination of these different questions. First, we shall consider the principal countries where pellagra is prevalent and the existing statistics with regard thereto. We shall next examine into the question, what are the conditions most favorable for toxic alterations in the grain, including the geographical distribution and seasonal appearances of pellagra? Then we shall give the results of the most recent microscopic investigations of ferments and parasitic moulds capable of altering corn and its products. We shall next study the clinical manifestations of the intoxication, and particularly its far-reaching complications for the individual, often leading to insanity and hereditary degeneracy. [Diagnosis, prognosis, prophylaxis and treatment will receive due consideration.]

*Synonyms.*—Alpine Scurvy, Asturian Leprosy, Asturian Rose, Disease of the Landes, Muñdismus, Psychoneurosis Mañdica, Mal de la Rosa, Mal del sole, Mal de Misère, and a great many others.

*Definition.*—Pellagra is an endemic malady which is characterized by an erythema upon the exposed surfaces of the body, by gastro-intestinal disorders and by nervous phenomena of toxic origin. It may terminate by severe cachexia or insanity.

“Pellagra,” says Dechambre, “is a food poisoning generally due to the use of spoiled corn, having the characteristics of endemicity in the countries where spoiled corn is consumed as food, and by epidemicity in the years and seasons in which the corn crop is most seriously damaged.”

*History, Geography and Relation to Corn.*—The appearance of pellagra in Europe goes back to 1720, the epoch of the introduction of corn planting.

[According to Babes and Sion it is probable that pellagra appeared in Europe long before its scientific description, but it was classed with such diseases as chronic intestinal and nervous conditions or mental disorders, or, again, as leprous or scorbutic manifestations. So it is difficult to determine whether or not the disease antedated the introduction of corn into Europe. In fact, there is no agreement among writers when the latter event took place. The first recognition and description of the disease is usually credited to Gaspar Casàl of Spain, 1735.]

The authors who claim to have found descriptions of this disease in these very regions anterior to this date have been deceived. For example, F. Frapolli erroneously believed he had found a picture of pellagra in the description of *la pellarella* in 1578, when as a matter of fact that condition was a syphilitic manifestation. [But to Frapolli we are



indebted for the introduction, in 1771, of the name pellagra, which is usually derived from *pelle*—skin and *agra*—rough. He is said to have found the word already in use among the people.]

The history of the progress of this endemic affection, reconstructed according to the successive medical descriptions in diverse regions, coincides with that of the extension of corn culture or of its importation and use. It is sufficient to recapitulate the principal works by date, by authors and by localities from 1760 to 1807.

1760-1779. Terzaghi, Moscati, Alberti—Upper Lombardy.

1771-1778. Frapolli and Zanetti—Central Lombardy and Milan.

1776. Odoardi—Upper Milan and Tessin.

1780-1786. Ghirlanda Gherardini—Treviso.

1788-1789. Strambio, Jansen—Central Lombardy.

1795. Allioni—Milan.

1790-1807. Frione—Venice and Corinthia.

1807. Cerri—Eastern Lombardy.

The geographical progress of the scourge from the center to the north and towards the east can be traced in this bibliographic-historic résumé.

Some apparent contradictions may be explained by going deeper into the examination. Thus, Greece, having already introduced the cultivation of corn, was found free from pellagra by Holland (1817); whereas, some regions to which Greece exported corn suffered from the malady. This resulted from the fact that the change in the grain necessary to

produce the disease had taken place during transportation; that is, from defective loading, rains and humidity.

As we shall see, the seasonal fluctuations of the malady in certain countries confirm these views. Indeed, we can verify their association, by comparing the official statistics of our time with the maps showing corn production, for example, in Italy, where the Minister of Agriculture has arranged these data in parallel columns.

In Abruzzi, where they have just begun to use corn as food, pellagra has as yet made very little headway; as also in Florence, and in Arezzo especially, as well as in Siena, where corn is little used. The very provinces where pellagrins are most numerous are those in which corn products are extensively used, as the provinces of Padua, Brescia, Cremona, Rovigo, Ferrara, Novara, Lucca, Venetia and Bergamo. Hence, we can no longer doubt a relationship between Indian corn and pellagra.

The counterpart of the above data is found in the instances where the cultivation and use of corn having been given up, pellagra has disappeared. After a philanthropist, Costa, introduced into certain localities of Italy the cultivation of lupines, which enrich the soil and permit the keeping of a larger number of animals, not only did the cultivation and importation of corn decline, but pellagra also.

It is interesting to cast a glance at the facts collected by observers in other countries, which agree in a general way with our own.



In Roumania, Felix states that pellagra has appeared in consequence of the continued use of mouldy corn as food. He incriminates particularly *Penicillium glaucum*, and *Puccinia segetum* and *nigricans*.

The Roumanian peasant recognizes that corn improperly harvested becomes covered with a whitish coating, that it has the taste of mould, and that soup made from such corn causes thirst and indigestion. It often happens, indeed, that it has no other consequences. These peasants suffer also from intermittent fever. They are badly housed and poorly nourished. Many of them are unable to sow their corn until very late; and they harvest it either too early or during the autumnal rains. They gather it then in little woven baskets which do not protect it from dampness, so that the grain becomes covered with mould and often actually decays. Roumanian infants are affected by pellagra as well as adults. Antoniu and Nicolaidi saw there a great number of little children who were pellagrous. The former of these authors has studied with especial care the pellagrous in the district where he is chief physician. He had under observation 500 pellagrins and considered *Penicillium* as the only cause of the malady. He reported cases among the well-to-do and robust inhabitants of the high regions of the district of Piatra who use milk and meat, but who are often obliged to harvest their corn before its complete maturity.

For the same reason the malady is observed in wealthy districts such as Nemtzu and Becan. The chemist Lendway who analysed the corn submitted by Antoniu as the cause of the malady, found it tainted with *Penicillium maidis* and not with *Sporisorium*.

Antoniou has made very interesting experimental studies with spoiled corn. Chickens fed on it for some weeks lost their feathers and drooped; in this condition they laid light eggs, having misshapen, porous shells with irregular surfaces, and they refused to sit on their nests. Dogs fed for six months on spoiled corn lost their hair and showed erythema.

While physician to a penitentiary, Antoniu found that the corn furnished for the soup of the inmates was spoiled. He selected from the prisoners four workmen and three robust young peasants, and had them fed all winter on nothing but corn gruel. In the spring he examined them carefully, and found that all of them had become pellagrous. The workmen, who were from the city, had been in the habit of eating meat and cheese besides the regulation dietary. Also a banker, who ate corn meal gruel every day as well as cheese, became a chronic pellagrin. When he changed his diet the malady disappeared.

The experience at Corfu is classical. There Pretenderis Thypaldos studied the history of the appearance of pellagra and the manifestations of the disease in the homes of 50 pellagrins. All had eaten spoiled corn. Some other communities, not



far from the villages where they lived, were free from pellagra, because in the latter millet and barley were eaten. In a village of Albanians where wheat-bread and fish were commonly eaten he found two persons affected with pellagra. They belonged to the poorest class and corn was their chief article of diet.

Thypaldos remarks that this injurious influence is not explained by chemical analysis, for though corn contains perhaps less nitrogenous substance than wheat, it always contains more proteid than rye, which does not cause pellagra.

Corn has been used for a long time in Corfu, but pellagra did not make its appearance there till within the last twenty years. Corfu has never been able to raise enough corn for home consumption. Additional supplies were imported from Epirus and Albania, equally as good as the home raised cereal, because harvested in the dry months. The peasants eat the unripe grain and expose the rest to dry in the sun, afterwards storing it in casks and grinding it later. Preservation is favored by the climate. Some years previous to these observations, very heavy rains had spoiled the corn crop. Later, in consequence of the extension of vine growing, the corn crop steadily decreased and it became necessary to import the cereal from Greece, Macedonia and the countries of the Danube, in addition to the supply brought from Albania. Because of the long sea voyage it always arrived at its destination in very bad condition. One community which had no pellagrins so long as it raised its own corn, now,



Plate I. South Carolina case. Symmetrical lesions of hands. Skin dry and exfoliating. Color dark. Courtesy of Dr. J. J. Watson.





having for seven years used imported corn, has nine of them to every six hundred inhabitants.

The ready decomposition of corn is explained by the great quantity of fat contained in its embryo, equalling 63 per cent. of its weight, or two-thirds more than the fat contained in rye. The embryo not having any perisperm is more exposed to the air. Thus corn, if damp, is more subject to mould than any other cereal.

[The percentage of fat given above is too high. According to Hopkins, Smith and East ("The Chemical Composition of Different Parts of the Corn Kernel"): "In corn of low protein content the embryos constituted 9.59 per cent. by weight of the entire kernel. The fat content of the embryos was 36.54 per cent., while that of the entire kernel was 4.20 per cent. In high protein corn the embryos constituted 11.93 per cent. of the whole kernel. Its fat content was 33.71 per cent., while the fat content of the entire kernels was 5.36 per cent." Joseph Schindler gives the following figures which are supposed to be averages for corn in the Tyrol: "Fat content of the entire kernel 4.2 per cent., fat content of the embryo 22.0 per cent."]

In Servia, Bulgaria and Roumania the number of pellagrins, which was 7,000 in 1894-5, was in 1906, according to Triller, 30,000\*. The same increase has been noted in Turkey in Europe, in Greece, in the Ionian Isles, in Asia Minor, in Tripoli, in Tunis and finally in Egypt. In Egypt, first reported in 1893 by Sandwith, pellagra has been observed by

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\*De la Pellagre, Th. de Paris, 1906.



Warnock, and on his recent journey by A. Marie. "The pellagrous affection," says Warnock, "attributed to the eating of spoiled corn is evidently spread over the greater part of Egypt. A portion only of the fellaheen become insane. The number of these pellagrous lunatics admitted to the asylum at Cairo can give only a feeble idea of the seriousness of the scourge. Sooner or later the government will have to take measures to combat its development." Furthermore, Warnock has noted at the Cairo asylum the presence of cases of insanity produced by pellagra.\* These statistics of the cases under observation at that asylum in recent years are taken from his annual reports:

YEAR	MEN	WOMEN	TOTAL
1896	9	2	11
1897	10	13	23
1898	10	29	39
1899	19	14	33
1900	8	27	35
1901	27	10	37
1902	23	10	33
1903	41	11	52
1904	38	15	53
1905	54	11	65
1906	46	13	59
1907	69	20	89
1908	71	17	88
1909	68	33	101
	<hr/> 493	<hr/> 225	<hr/> 718

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\**The Journal of Mental Science*, January, 1902.

## DEATHS FROM PELLAGRA AT THE CAIRO ASYLUM.

YEAR	MEN	WOMEN	TOTAL
1901	6	4	10
1902	6	2	8
1903	9	1	10
1904	3	3	6
1905	13	4	17
1906	9	1	10
1907	7	2	9
1908	6	2	8
1909	10	5	15
	—	—	—
	69	24	93

In Spain, according to Triller, despite prophylaxis, pellagra today affects 20 per cent. of the inhabitants of certain provinces. Casàl, who first, in 1735, described pellagra in the Asturias, speaks thus of that severely tried people:

"Corn is the principal food of the laborer there; soups are made of it to which they usually add milk; likewise they eat eggs, fish and cheese; very rarely they buy fresh meat and occasionally salt meat."

Here, as elsewhere, they began by misconceiving the real origin of the affection.

Roel tried to prove that pellagra came from leprosy. But he recognized that pellagrins lived on corn.\* Furthermore, he estimates that corn was imported to the value of 13,000,000 francs (or about \$2,600,000), and of this 5,000,000 francs (\$1,000,000) worth was imported by sea, but corn imported by

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\**Etiologia della pellagra*; Oviedo, 1880.



coastwise vessels is always damaged either by salt water or by rain.

In Mexico several authors, among them Iturbide, have described erythemas combined with nervous troubles and gastro-intestinal disorders analagous to pellagra. But these cases have been questioned\* and appear to have been confused with other affections from which true pellagra ought to be distinguished, but with which it can, however, be associated, as has been observed. An example is syphilis, which, combined with pellagra, may have caused the diseases reported from Mexico by Contreras and del Pinto (R. Sandoval and G. Tellez).

In Ireland also they eat a great deal of corn, but it is put up in granaries and preserved by the Devaux system. (See page 324.)

In France pellagra belongs to history, being a memory only, or very nearly so, since it has not figured for a long time in asylum statistics. Formerly, however, it was a different story. Savoy, after its annexation to France, kept up for a long time the dietetic habits of northern Italy; but the use of corn meal has greatly declined in Savoy since 1860. In the poor districts of the Pyrenees and of the Garonne basin and in the Landes, where Spanish influence prevails, the use of a corn dietary persisted up to the middle of the nineteenth century. Nevertheless, it was a mixed dietary that was incriminated by the investigating commission and its secretary, Théophile Roussel, who noted that the epidemic exacerbations of pellagra coincide with

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\*Vide Colndet, 1869.

the seasonal periods when much corn is used, while both meat supplies (mutton, pork, fish) and vegetables (millet, rye, cabbage, pumpkins) are scarce. Actually, the little corn now consumed in France is of a better quality and well prepared. Hence pellagra has disappeared. [It is not to be forgotten, however, as is pointed out elsewhere, that the disappearance of pellagra also coincided with a general amelioration in the lot of the peasantry.]

Since the first communications of Jean Hameau to the Royal Society of Medicine of Bordeaux in 1829, up to 1880, observations, investigations, reports and publications of every kind have followed one another without interruption. Learned societies, medical journals, Italian and French, the oldest French review of psychiatry (*Les Annales Médico-Psychologiques*), have been filled with interesting observations on this subject. But, as Régis remarks, silence quickly followed in France, and for the last twenty years only a few cases have been reported, even from the region of Bordeaux, where the pellagra of the Landes has justly stimulated inquiring minds for a half century. What has happened? And how shall we explain this sudden change? Is it that pellagra has disappeared from the Landes, or have the people become accustomed to it and lost their interest in its ravages, after having once been so much concerned? The response to this interesting question has been given by Régis himself\* in no uncertain manner, and we are permitted to say after





his last researches that pellagra does not exist any longer in the French Landes.

As far back as 1879 Desmaisons, in his report on pellagra in southwestern France, drew conclusions showing the decrease of this endemic disease; and since that time the opinion generally entertained, and expressed in works like those of Dupuy and of Chambrelant, has been that this decrease has become more and more pronounced.

At the asylums at Pau (St. Luc) and at Auch, the researches of our colleagues have furnished confirmative results. "During the period of thirty years," says Girma, "from 1875 to 1905 inclusive, we have admitted 26 pellagrins, of whom 13 were men and 13 women, and of these the last case dates back to 1895. These patients were all Landais, except 3, who were originally from Basses-Pyrénées, upon the confines, however, of the Landes. It is only among the poverty-stricken that pellagrous manifestations occur. The annual average of the admissions of Landais from 1876 to 1905 was 33. In a total of 811 admissions 23 pellagrins were found. The symptoms of these insane pellagrins were almost always those of melancholia. Sometimes a rather short phase of violent excitement, suggesting acute delirium, has been observed, but a stage of melancholia followed the agitation, terminating sometimes in death, sometimes in recovery."

Dr. Chevalier-Lavaure no longer observes pellagra in the asylum at Auch; but further inquiry should be made to learn from the antecedents of these insane patients whether or not pellagra is hereditary.

"Pellagra," adds Régis, "has almost totally disappeared from the Landes during the last fifteen years." We shall return to this disappearance of the pellagrous intoxication from France in order to explain the conditions of prophylaxis and of the extinction of pellagra elsewhere, for, unfortunately, it exists, and to a very serious extent, in numerous other countries at the present time.

Confronted by these demonstrations and arguments as to the cause of pellagra, how can we account for the persistent negligence of governments and of the public regarding its spread?

It is because the public is hard to be convinced. The love of life appeals, then cupidity conquers the love of life. The renowned teachers in medical centers do not live in the country, and being city dwellers, they do not appreciate the real gravity of the situation. Moreover, the few good observers living in the country, are too systematically led astray by ignorant people. Pellagra is sometimes hereditary, and thus does not originate directly from damaged corn; sometimes it shows itself in persons affected with malaria, alcoholism, puerperal disease, or from the consequences of depressing affections, and then it is easy to invoke a determining cause other than corn, if the symptom-complex should be misinterpreted.

In those regions where pellagra is just beginning to manifest itself, but has not yet involved a large part of the population, as for example, near Rome, or near Perugia, it is easier to discern the causes of it, than in places like Milan and Bergamo, where the

disease has persisted for a century, but is carefully concealed by the persons who are either responsible for it, or connive at its development. As Jacini has said, cupidity and ignorance lead man to the worst actions; the least scrupulous can make excuses. Many even believe they do right in giving damaged corn to their workmen, because in this way they can feed their help at less expense. But if they knew that they were thus giving them not only an inferior food, but a veritable poison, they would doubtless abstain from doing so. Few persons are convinced that moulded corn is truly a poison; or if they have heard that the fact has been demonstrated by experiment, they also know that several well-known authorities have combated this hypothesis, and have been able apparently to refute the maize theory.

When Marzari (1810) incriminated corn as the only cause of pellagra, all his confrères attacked him; and the great Congress of Medical Societies of 1859 approved their attitude. The Royal Institute of Sciences of Lombardy, in 1874, officially opposed Lombroso's teaching by declaring moulded corn to be harmless (*Relat. Biffi*).

In many regions corn, originally from Mexico[?], a country with a dry climate, is harvested either prematurely or late. In such countries it is frequently gathered after the rains of autumn have inundated the fields and barns; or else, exposed to sea water and rain in coasting vessels, it is spoiled during transportation. In upper Italy the barns are often so poorly built that the rain penetrates and, consequently, moulds develop on the harvested

grain; then with the heat of summer the corn, which is insufficiently aired, rapidly decomposes. Often also the miller passes steam over the meal in order to increase its weight, a process which renders it damp and again prepares the way for mould.

Still more injurious is the custom of making with bad meal large round cakes of which the portion just within the crust is scarcely cooked while the interior remains sodden and rapidly decomposes. There are also the fraudulent processes practised by the bakers who, in the country, are often protected by the local officials.

That there is a correlation between the increase in the number of pellagrins and great humidity has been proved for Venetia especially. Parallel statistics have been prepared showing the rainfall and epidemic manifestations of pellagra; and these are found to coincide from 1877 to 1888. Cloudy weather is also a factor of influence in upper Italy, especially in the provinces of Venetia and of Udine, in favoring the development of moulds. All facts conspire, therefore, to show that the provinces of Venetia, Udine and Treviso have a climate in which corn cannot reach maturity and, in consequence, easily becomes the medium for parasitic growths in which the flora of these provinces is particularly rich.

Let us now see what are the principal objections to the hypothesis of spoiled corn as a cause of pellagra. They have been numerous, but can be reduced to these three: cupidity, ignorance and deep poverty. It cannot be disputed that pellagra is a



disease of helpless poverty, developing from objectionable food, from grain itself badly sown, badly harvested, badly preserved or badly transported and prepared. Abject poverty is indeed a cause of eating spoiled corn; and the objection that such poverty is a necessary preliminary does not hold good, though the geography of pauperism coincides in certain respects with the distribution of pellagra.

When polenta [a mush or porridge made of corn meal and universally eaten by the peasantry of northern Italy] is fresh, says Miraglia, the family remains well; whereas, pellagra makes its appearance when a great potful of polenta, enough to last the family a week, is made at one time of soured meal. This is done in certain regions by the poor and ignorant. Corn is thus liable to become harmful after its preparation for use as food. In many districts around Parma the use of bean cakes saves the people from pellagra, which prevails so extensively in the neighboring territory of Reggio.

At Chieri, in Piedmont, since the development of the weaving industry, the amelioration of living conditions has extended even to the country districts, so that the small farmer is living better; and if hereafter he continues to feed the damaged corn to the hogs pellagra will diminish. In Calabria, Pasquali has, it is true, found moulded corn, but the farmers, being prosperous, do not eat it when spoiled. However, a new source of pellagra has manifested itself in the district of Girifalco since the introduction of corn bread. At Cava Carbonara there are no pellagrins, while in the neighboring communes they are

numerous, but from this territory there is a great emigration at one season, followed by a later return with savings, which permits the people to enjoy wheat bread and good corn bread. Near Pavia, two villages exposed to frequent inundations have the same climate and the same soil; the one, Santa Zenone, is in the hands of numerous small proprietors who rent to their farmers on favorable terms—there no pellagra is found. At Pieve, Porto-Morone, on the contrary, the land is in the hands of large proprietors; high rents force the peasants to eat corn and to deny themselves pork and beef; and so the disease is prevalent.

In the neighborhood of Rovigo the terms of land rental are favorable. The laborer there may secure a piece of land for his own use. There is found there, nevertheless, a certain quantity of spoiled corn, which, however, is not eaten by the peasant. The pay of the day laborer is significant from our point of view, as we shall presently see. In the vicinity of Brescia are two villages, very near together, Rovato and Cuzzago. The one has a very fertile soil and the other very poor; in the former the system called *schiavatico* exists, which pays ludicrously small wages per day; in the latter, the proprietors, in order to rent their holdings at all, let the small farmers have a third of the annual yield, and this is why they are enabled also to raise barley, rye, etc. So the peasant then is in a situation which permits him to live better. It is in this way that the poor return of the soil preserves him from the malady of his corn-fed neighbor. At Gardone pel-

lagra prevails proportionately with the control of land by large owners; a small crop of corn is dried easily; a large one, with difficulty, and it therefore spoils more easily. This is the reason the large landed estates, controlled by wealthy landowners, are here the cause of the propagation of the disease.

The *quarantina* (forty-day crop) is the product of the last harvest of corn made in autumn, which the Italian proprietor leaves to his farmers, or to his day-laborers. This corn is hung on the outside of the huts and rarely dries as it should; in damp years it decomposes quickly.

Imported corn, damaged by salt water, costs five francs\* a bushel (*boisseau*), while good corn costs nine. In the villages often inundated by the Po, dampness is almost constant, so that after harvest the corn is always spoiled; frequently, also, the harvesting is done before complete maturity. Corn is, therefore, never eaten in that region except in bad condition.

As it is difficult to sell unsound cereals, they are consumed where grown, and the preference is, of course, to assign them to the peasantry.

When the division of the crop is made between the proprietors and the small farmers, the latter are compelled to accept a certain quantity of bad corn, and they are not in a position to decline a variety of food which neither they themselves nor the farm managers regard as poisonous.

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\*The author throughout seems to use franc and lira interchangeably; and since, for all practical purposes, the value of each is about the same, twenty cents, we have also used them interchangeably. The same may be said of centime and centesimo, each being worth about one-fifth of a cent.

The Piedmont Commission on Pellagra has very properly cited Biella as a place free from pellagra in spite of a large consumption of corn. In this industrial town of upper Italy the workman is so well paid that he refuses to eat polenta, or bread made of damaged corn. The economic improvement at Biella has, therefore, caused pellagra to decrease, but this has been done by removing the necessity of eating spoiled corn.

Near Innsbruck the corn is dried on the interior of houses upon a kind of screen which extends from the roof to the ground. The corn being dried by this method, the people know nothing of pellagra. But still this is possible only for the small land-owners.

Around Pavia pellagra is little known, because ovens are in use for drying the corn; rice, too, is cultivated there, and they make bread of it. Although this has not so good a taste, it has also not the disadvantages of corn bread.

In the territory of Brianza pellagra is endemic because, though the soil is dry, the grain is stored in silo-like pits made of beaten earth.

In certain communities the heredity of pellagra is a cause of degeneracy still more destructive than the eating of damaged corn. So it is at Colla, near Reggio, at Inverno, near Pavia, at Dolce and at Rivoli, near Verona, at Sermide, near Mantua, where almost all the families are affected by hereditary pellagra, and one can no longer say that the malady is due to the direct influence of corn. This situation, which has often been concealed for shame,



has complicated the researches in regard to the etiology of the disease, for men were seen to become pellagrous who no longer ate corn, and who often were rich, but suffered from the consequences of an hereditary vulnerability.

Together with the abject poverty, the ignorance, vanity and credulity of the poor consumers must be reckoned the dishonesty of the farmer-merchants. One can find spoiled corn in all the granaries and in all the great grain markets, as also in the communal warehouses, but one does not find it unless he is warned, so to speak, to conceal all appearance of distrust. If the farmer suspects that an inquirer comes officially or officiously, he will sell to the merchants in order to hide the basis for making a report to the sanitary police. Many a time at the beginning of his investigations one of us had reason for reporting this fact:

"Having heard that a great quantity of Roumanian corn had arrived at Ancona, I asked for two sacks of it. The dealers replied in fear that the corn had to be inspected by the sanitary police; that they would not sell just two sacks, that it was necessary to call for fifty at least. It is for this reason that at Sissa the official Commission on Pellagra arrived at the conclusion that there did not exist any connection between the malady and the consumption of corn, for the countrymen of Sissa were accustomed to eating only corn of the best quality. When I went there I found in common use a meal of Roumanian corn which was completely spoiled and was sold at a low price. I had the Parma Board of Health informed of it, and when these gentlemen did not wish to believe me, I conducted them to two of the largest corn merchants, who offered us some hundreds of sacks of it because we had assumed the role of merchants."

When one appears as a representative of Boards of Health there is naturally never any spoiled corn for sale. Besides not infrequently corn offered for sale is made to appear of good quality because the merchants, and even the peasants, have learned the trick of manipulating it with plaster in such a way that its defective grayish spots are concealed. Often, also, the bad corn is at the bottom of the sack or mixed with the good. When fraudulent manipulation is not done with the unground cereal it is done with the meal by the millers. The buyer does not then observe anything unnatural, and consequently cannot trace the cause of his illness.

How can any one be astonished that the peasant does not discern the cause of pellagra, when one knows that the peasant himself misconceives more or less conscientiously and conceals from the physician the causes of other maladies, such as syphilis, scrofula, etc.? His errors were, otherwise, those of the metaphysicians, of which they are the remote popular survival. It is thus that today the people believe in the herpetic, scorbutic and solar etiologies as held by the physicians of old. In the neighborhood of Verona the peasants claim that pellagra comes from the rays of the sun, which burn the skin; at Parma they attribute it to the damp air; at Vicenza to eczema.

Vanity also plays its part. Near Vicenza, for example, the physician, for his own sake, needs to take care not to say to a peasant that he has pellagra. "The patient has the salt rheum," or "an accidental eruption"—but never "pellagra." In this region the



term is synonymous with insanity, and for this reason no one will admit having it even in a mild form.

The poor peasant, full of vanity, as all mortals, wishes to pretend that he eats wholesome food, at least wholesome corn, which is his staff of life, and he denies that he eats it spoiled, because he feels ashamed of his poverty, or, indeed, because he feels responsible himself for the bad preparation of his food. On the market and in the granaries of Villafranca there is no lack of cheap corn, which has been gathered prematurely. An explanation is that the laborers stole it from the landowners by sackfuls from the field and sold it, or, it may be, concealed it for their own use. It is such corn, dried too late, that easily moulds.

But often the peasant does not realize that this change has taken place, for his attention has not been called to it. The diverse symptoms of the beginning of the chronic disease confuse him. Some are even so ignorant that they add spoiled corn to their meal, because of its piquant and aromatic taste. Certain persons contend that spoiled corn facilitates their digestion. For instance, Costallat, in the Landes, has seen bread seasoned by spurred rye because of its peculiar flavor.

Sometimes a district, in spite of the exclusive use of corn, remains free from pellagra. This is because there are local reasons which prevent its development. Jacini observes, for example, that pellagra appeared late in the mountains of Lombardy, because the difficulties of transportation kept up higher prices there; an expensive article of mer-



**Plate II. Illinois case. Pellagrous "glove." Courtesy of Dr. G. A. Zeller.**





chandise can not be sold if of bad quality. Up to his time they did not import corn from the ports of the Black Sea. Later, because cheap, this corn gained entrance, but was not used in the mountains at first except as food for hogs.

We always discover in the final analysis the reciprocal relation which exists between poverty and the causes which are recognized as essential for the toxic alterations of corn, namely: the extension of its planting, defective transportation over the sea and the humidity of mountain climates.

[In this connection it may be pertinent to refer briefly to a universal inquiry now being made in the United States as to whether the more or less recent appearance of pellagra here can in any possible way be explained by changes which have taken place, in recent years, in methods applied to corn culture, etc.

McCampbell\* has suggested that in the Southern States when harvesting corn the old and better practice of "topping" has been largely replaced by that of "cutting and shocking," and that this latter method may produce better conditions for spoiling of the grain.

Alsberg, of the Department of Agriculture at Washington,\* disclaiming any intention of expressing an opinion on etiology, has recently discussed at some length this entire question.

With regard to the Southern States he shows that a great deal of corn is consumed there; that

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\*Confer. on Pellagra, Columbia, S. C., 1908.

\**N. Y. Med. Journal*, xc, 2, 50.

an insufficient supply is grown for local consumption and a great deal is in consequence imported from the corn belt. So far as Southern agricultural methods are concerned, the varieties of corn planted have been much changed; and the adoption of the principle of "rotation of crops" has caused a tendency to discontinue the old practice of "topping" and to resort to that of "cutting and shocking," which often results in harvesting the grain prematurely, and probably places it under very much more favorable conditions for spoiling. He also points out the difference in the process of milling between the Southern States and other sections. In the latter the germ, which is the part of the grain most easily spoiled, is almost entirely separated and is discarded, while in the former it is ground in with the meal.

With regard to methods in the corn belt, he states that the varieties of corn planted in the last decades have changed greatly, with a constant tendency towards increasing the oil content of the grain. Most of the oil is in the embryo and this part of the grain is most subject to change (moulding). Hence grain with a large embryo not only spoils more readily, but if spoiled, its toxic content would, of course, be greater. In speaking of climatic conditions, he says that of late years there have been in the corn belt a series of cold, wet falls which have probably done a great deal to prevent proper ripening of the corn. He also points out the dangerous extension northward of corn culture to climates not suited to its proper growth, and questions whether,

with existing varieties, the northern limit of safe corn culture has not already been exceeded. The storing of the crop, too, has not always been properly looked after, and economic conditions have frequently begotten a temptation to harvest the grain prematurely. With regard to transportation, he comments on the folly, when shipping to warm climates, of using closed cars without ventilation, thus producing ideal conditions for over-heating and fermentation.

Finally, Alsberg thinks that probably the most potent factor in the spoiling of corn is the water that is usually present, and suggests as a remedy a system of federal grain standardization.]



## CHAPTER II

### GENERAL STATISTICS.

Strambio in 1784 calculated that nearly one-twentieth of the population was pellagrous. In districts worst affected by the malady there was estimated to be one pellagrin in every five or six individuals. By 1819 the proportion was increasing daily.\*

Visiting the hospital for the insane in Milan, Holland (1817), among five hundred lunatics of both sexes confined in this establishment, found more than two-thirds of them to be due to pellagra. At Udine in 1883 there was an enormous recrudescence of pellagra, and the investigator Zinio, who traveled personally from place to place, reported that during the inundation of 1882 the inhabitants of the country districts found themselves face to face with the necessity of eating spoiled corn. At Sissa, the official Investigating Commission reporting on the question of the increase of pellagra stated that the inhabitants fed exclusively on *meliga*—a mixture of *quarantino* and damaged corn meal imported from America.

Inundations favor also the contemporaneous recrudescence of the swamp fevers, which coincide sometimes with pellagra, the development of which they favor by diminishing the power of resistance in malarial subjects. According to the prefectorial report of Sondrio it appears that in 120,000 inhab-

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\*Dictionnaire des Sciences Médicales, 1819, pp. 85 and 89.

itants there were 71 pellagrous, scattered among nine villages where malaria was endemic. The same observations were made in the plains of Bergamo and at Valcamonica, near Brescia.

In Umbria, Adriani found the largest number of pellagrins in the neighborhood of Perugia—278—while at Foligno there were only two, at Orvieto nine, at Spoleto four, at Terni four and at Rieti none. The cause of this predominance of pellagrins around Perugia is the constant deforestation of the region which augments humidity and thus facilitates the decomposition of the corn.

Lack of cleanliness in their dwellings is not a cause of the development of pellagra, since cases are numerous among peasants who keep their houses very neat. Likewise, the deprivation of wine is not to be reckoned as a causative factor, for in the years when wine is abundant and very cheap pellagra increases. Neither does abject poverty seem to enter as a direct factor in the increase of pellagra when it does not lead its unfortunate victims to the use of corn of dubious quality. In the neighborhood of Perugia the soil is extremely fertile; it is, furthermore, cultivated generally by half-renters and on good terms. Some of them, nevertheless, have pellagra. They are not poor, but they are avaricious.

There is a relation between bad harvests and the increase of pellagra; nevertheless, one cannot deny that abject poverty also favors indirectly the increase of the malady. The fact is that pellagra does not affect the poor alone, but also people in easy circumstances, though it extends much more rapidly among the poverty stricken classes.

Adriani asks why pellagra appears always in the country districts and never among the poor inhabitants of the cities. This is because the peasant alone consumes the spoiled corn. Many give damaged corn to their laborers because when it has a bad odor they eat less of it; or, indeed, if they refuse it, they are deceived by an admixture of the good. The millers also, as we have seen, resort to the tricks of the trade.

The poorest part of the population, deprived of cooking utensils, stoves, etc., and not knowing other modes of preparation, make for themselves with meal half-cooked corn cakes; even when made with meal of good quality these cakes rapidly undergo deleterious change. Their dietary includes also beans, different kinds of vegetables and sometimes acorns. In summer it is the custom to soak in soup the bread made from spoiled corn meal, as Adriani has shown in his investigations.

That there is a relation between the importation of foreign Indian corn and a recrudescence of the disease should not be doubted for a moment. In the region of Perugia a harvest having been very bad, the land owners and the managers of the great estates supplied their renters and laborers with imported corn. The number of pellagrins increased in an alarming manner, and chiefly where foreign corn had been most used. That year, of 125 admissions to the insane asylum of Perugia, 49 were cases of pellagrous insanity.

The influence of an Indian corn dietary is manifest also in the regions of Udine, Palma and



Districts.	Pellegrins and Their Occupations, 1878.				Production of Corn by Quintals According to the Investigation of 1878.	Number of Communes in Which Pellegrins Ate Spoiled Corn.			Suicides from Pellagra.	Number of			Population, Census of 1871.
	Small Land-owners.	Day Labor-ers.	Yearly La-borers.	Total.		Often.	Almost Never.	Sometimes.		Total Com-munes.	Communes Infected with Pellagra.	Immune Communes.	
Udine .....	83	167	10	260	157,021.05	4	8	1	1	15	13	2	67,980
San Daniele .....	47	113	4	164	59,962.77	1	4	1	...	11	8	3	28,668
Spilimbergo .....	20	62	9	91	61,506.82	2	4	2	...	12	8	4	32,169
Maniago .....	43	8	...	52	29,380.14	...	1	3	...	11	5	7	21,986
Sacile .....	52	114	22	188	39,104.54	1	1	1	2	11	5	...	20,089
Pordenone .....	321	196	95	612	141,688.55	1	9	2	2	14	13	...	55,489
San Vito .....	212	541	378	1,131	66,590.74	2	4	2	2	10	8	2	8,404
Codrolopo .....	144	335	37	556	66,493.30	2	2	1	2	7	7	...	21,485
Latisana .....	103	103	53	163	50,185.04	1	5	...	...	8	3	...	17,136
Palma .....	66	255	165	487	48,841.30	9	3	...	...	11	10	5	26,592
Cividale .....	22	91	12	125	89,176.27	1	8	...	1	14	8	6	38,591
San Pietro degli Slavi .....	...	...	...	...	19,026.49	...	2	...	...	7	2	3	14,051
Moggio .....	8	...	...	8	20,854.47	...	...	...	...	8	...	8	12,890
Ampezzo .....	...	...	...	...	18,583.50	...	...	...	...	8	...	...	10,674
Tolmezzo .....	...	...	...	...	55,192.64	...	...	...	...	20	...	...	32,882
Gemona .....	7	38	2	47	68,617.07	...	4	2	...	8	6	...	27,972
Tarcento .....	25	45	1	71	42,427.90	1	5	1	2	10	7	3	25,776
Totals .....	1,057	2,063	838	3,953	2,029,662.59	21	52	21	8	179	102	77	461,584

Frindi. There a single village, Marano, is entirely free from pellagra. It is inhabited by 210 families, who, with the exception of 26 employees and families of traders, live largely on fish (using each year 2,600 quintals\* of fish and eating no corn). Opposite, at Sesto, which has 3,700 inhabitants, 700 being pellagrous, they use 1,500 quintals of Indian corn imported from foreign countries, while at Cassarsa the same number of inhabitants consume only 800 quintals of corn, and there are there only 90 cases of pellagra.

The relation between pellagra and nutrition by damaged corn meal is very apparent according to comparative statistics tabulated for 94 communes inspected. In 42 polenta made with spoiled corn meal was largely consumed. It was also in evidence several times that the polenta meal was badly ground and the broth not well cooked. Out of 3,964 pellagrins, 1,022 declared that they often ate spoiled polenta, 1,383 sometimes, and 1,385 never. (See table). Manzini, to whom we owe this information, also made investigations in other villages to learn why they used such food. In seven communes it was declared that the corn meal had fermented; in seventeen that poverty forced them to buy only damaged corn meal, because it was very much cheaper; in sixteen, because it was harvested before maturity and badly cooked; in thirteen, because the corn was sown on swampy ground, or harvested during a damp autumn when they were without the means for drying it.

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\*A quintal is 100 pounds.

At the asylum which we visited the admissions of patients for pellagra for the years 1896 to 1906 was as follows:

Year	Men	Women	Totals
1896.. . . . .	9	2	11
1897.. . . . .	10	13	23
1898.. . . . .	10	29	39
1899.. . . . .	19	14	33
1900.. . . . .	8	27	35
1901.. . . . .	27	10	37
1902.. . . . .	23	10	33
1903.. . . . .	41	11	52
1904.. . . . .	38	15	53
1905.. . . . .	54	11	65
1906.. . . . .	46	13	59
Total.. . . . .	285	155	440

Six large communes of Piedmont have officially declared that damaged corn meal is the cause of pellagra. In other communes it has been charged to the unhygienic condition of the dwellings, to nourishment on unripe corn, or, indeed, to its change in consequence of frequent storms.

The Miraglia investigation revealed the fact that many communes had tried in vain to prevent the use of spoiled corn meal. At Ivree it was asked: "How can we prevent the people who have harvested nothing but Indian corn from eating it? Hunger is even more terrible than pellagra." At Polesella: "No measure of the sanitary police can prevent the poor people from eating the spoiled corn meal which is sold to them."

At Rome it is well known that the inhabitants of the country eat every winter meal made from waste

corn. In the province of Ferrara the country people eat habitually spoiled meal; at Rovigo, as also in many Venetian villages, they eat damaged corn imported from foreign ports.

At San-Apollinario (again according to the investigation of Miraglia) the laborers compel the proprietors to take good corn in exchange for that which is damaged; at Piacenza they complain of the bad quality of the Hungarian corn; likewise at Arezzo and at Siena. At Città della Pieve, Lucca and Chioggia, the proprietors have the corn sorted and, instead of the good, give the waste to the laborers (Miraglia). At Costigliole, a village near Asti, in a region which is perhaps exempt from pellagra because it is rich in wine, Dr. Piccinini found a case of the disease in a peasant in good circumstances who ate meat and in whose case, consequently, it could not be a question of insufficient nourishment; but he also ate spoiled corn meal which he could not sell.

Balestra relates in his work upon the Campagna Romana that pellagrins are found on certain farms where the people do not eat the corn grown upon the dry soil of the Campagna, but spoiled imported corn. In the district of Mantua thirty-three persons declared that corn spoiled because they harvested it in autumn and because it was shocked on the damp ground; it then dries a very little, or even not at all, and in this condition it is threshed on the bare ground. At Sermide pellagra has increased because they are not only absolutely without ovens for drying the corn, but also without any sort of arrangement



for aeration. The corn is brought up to the unpaved areas for drying; these areas are never repaired; the peasants do not give proper attention to the drying process, while the majority of laborers are compelled by necessity to have the meal ground as quickly as possible. The commission made special inquiry whether the corn consumed by the peasants and principally by the day laborers was always thoroughly ripe and sound. Thirty-nine communes responded affirmatively; 14 communes replied that the corn was not always mature; in bad years they used imported corn of inferior quality, or perhaps the day laborers bought it of the millers who habitually sell the cereal damaged. It happens sometimes that persons having received good corn in payment, re-sell it in order to buy cheaper. Twelve communes declared that corn was often defective because it was harvested before maturity, or poorly dried, or preserved in damp warehouses.

It is noteworthy that where pellagra prevails it diminishes rapidly as soon as vigorous remedies are employed, or the commune establishes suitable drying machines.

For the last few years, in the province of Bergamo, there has been one pellagrin to every 107 inhabitants; in the province of Milan one to every 154; at Brescia one to every 41; at Cremona one to every 24. Since then the disease has spread considerably—in Valtellina, in Umbria, in Abruzzi, and even up to the neighborhood of Rome. In Lombardy the number of pellagrins rose in 1839 to 20,282; in 1856 it reached 38,777, and went to 40,838 in 1869.

In Venetia there were 20,000 pellagrins in 1853 and 1856, and 29,830 in 1879. The sanitary investigation by the government in 1886 and the preceding one of Miraglia\* showed that the number of pellagrins in Italy increased from 97,855 in 1879 to 104,067 in 1881. During these two years the disease was more prevalent in Lombardy and in Venetia, and much less in Piedmont, in Emilia, in Marches and in Umbria. Some sporadic cases appeared in Liguria and Latium.

It was in 1881 that the first four indubitable cases of pellagra were recognized in southern Italy—in the provinces of Teramo, Aquila, Chieti and Avelino, as also several doubtful cases in the provinces of Caserta, Benevento and Catanzaro.

In 1883, 6,025 pellagrins were treated in 866 civil hospitals, of which number 923 died; in 1884, 6,944 were treated in 993 civil hospitals, with 780 deaths; in 1885, 6,982 pellagrins were under treatment.

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\*Relazione sulla pellagra in Italia. 1884.

The table below\* shows the proportional mortality rate from pellagra in every 10,000 deaths, from 1881 to 1887:

Districts.	1881.	1882.	1883.	1884.	1885.	1886.	1887.
Piedmont. . . . .	77.1	70.9	58.0	39.1	46.4	36.9	24.3
Liguria. . . . .	4.1	1.4	4.1	12.0	5.3	2.3	.....
Lombardy. . . . .	387.8	319.4	251.3	208.7	195.2	157.4	92.6
Venetia. . . . .	633.4	500.2	397.4	323.4	313.5	374.8	251.7
Emilia. . . . .	290.6	214.7	143.0	108.4	121.6	116.6	79.5
Umbria. . . . .	71.9	63.6	34.3	29.1	24.8	53.8	52.5
Marches. . . . .	50.3	48.0	55.1	48.8	81.0	73.0	60.9
Tuscany. . . . .	68.4	62.2	38.8	37.9	49.4	37.0	29.9
Latium. . . . .	2.1	.....	.....	.....	2.0	2.9	.....
Abruzzi and Molise. . . . .	.....	.....	.....	.....	2.3	.....	.....
Campania. . . . .	0.8	.....	.....	.....	.....	.....	.....
Puglia. . . . .	.....	.....	.....	.....	.....	.....	.....
Basilicata. . . . .	.....	.....	.....	.....	.....	.....	.....
Calabria. . . . .	.....	.....	.....	.....	.....	.....	.....
Sicily. . . . .	0.4	.....	.....	.....	.....	.....	0.4
Sardinia. . . . .	.....	.....	.....	.....	.....	.....	.....

\**Statistica Sanitaria, Ministero Interno, N. 1890, Roma.*

These statistics show the distribution of pellagra in Italy and also show the disease at its maximum in Venetia, Lombardy and Emilia; and at its minimum in southern and insular Italy. For certain places there seems also an indication of an increase in numbers, with a *diminution of intensity in the last four years of these statistics.*

These statistics are clearer for smaller territory. Thus, there were in the department of Udine in 1878 (with 181,386 inhabitants) 3,964 pellagrins, against 2,000 from 1858 to 1859.

In the region around Lucca, Ceru found 896 pellagrins in the period 1871 to 1875, and the number was increasing every year. In the region around Mantua the disease is likewise on the increase, for against 1,228 cases in 1830 there were 2,195 cases in 1856, and in 1897 the number rose to 2,900.

The figures become still more striking when we compare them with those of the pellagrous insane, where each case passes through a series of medical examinations before admission into an asylum.

Pellagrous insane in Italian asylums:

December 31, 1877.....	1,348
“ “ 1880.....	1,742
“ “ 1883.....	1,746
“ “ 1884.....	1,723
“ “ 1885.....	1,741
“ “ 1886.....	1,487
“ “ 1887.....	1,342

The statistics of Lolli and Lombroso on the admissions into the insane asylums of Pesaro and Imola,

give for the period 1863 to 1872 the following figures:

	Forli and Imola	Pesaro	Ancona	Bologna
1863	13	..	..	64
1864	21	..	..	15
1865	21	..	..	27
1866	19	..	..	44
1867	29	..	..	44
1868	31	..	..	..
1869	48	16	8	..
1870	45	6	5	..
1871	33	13	6	..
1872	89	15	1	..

In Emilia in the years of 1873 to 1877 the number of pellagrous insane showed the following changes:

	1873	1874	1875	1876	1877
At Modena.....	38	48	16	17	31
At Reggio.....	63	85	18	20	41

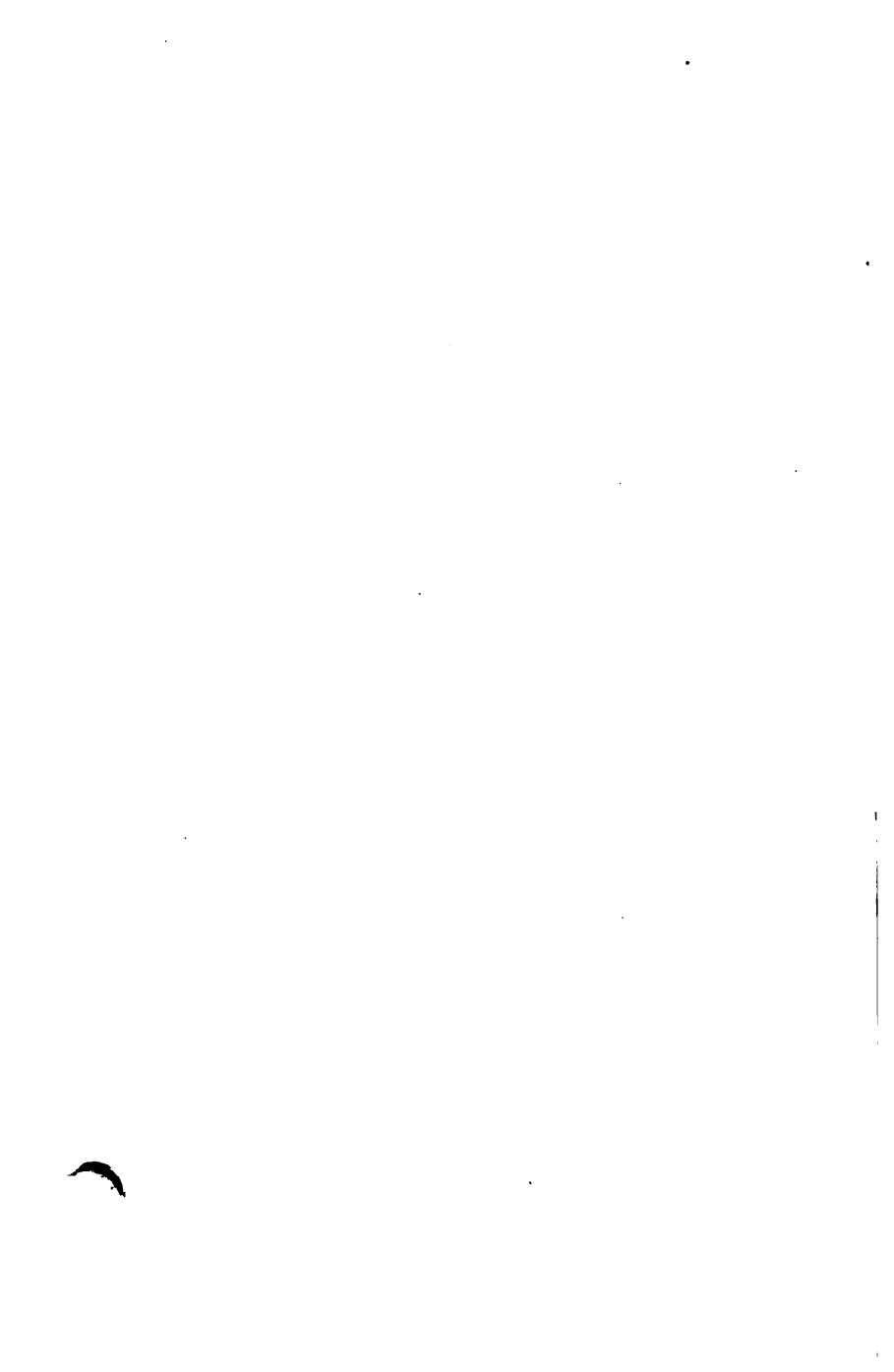
One thousand two hundred and sixty-three pellagrous insane were received into the asylum of Mantua from 1869 to 1877—consequently an average of 140 a year. During the first five years the average was 124; in the last four years it rose to 161.

Neusser reports 1,068 cases of pellagra in the Austrian Tyrol, in 1886, among 35,688 inhabitants, that is about 3 per cent. of the population. Of this number 96 pellagrins showed psychic disturbances, that is, 9 per cent.

During their visit to the International Congress of Milan (June 7, 1906,) the authors of this work had the honor of being received at the asylum of



Plate III. Egyptian case. Dry dermatitis on face, hands, neck and upper chest.  
Courtesy of Dr. R. G. White.



Mombello, where they were able to examine a number of pellagrous insane; they used the opportunity to compile complete statistics of these patients from 1879 up to 1906.

**PELLAGROUS INSANE ADMITTED FROM 1879 TO 1906.**

Years	Men	Women	Total
1879.. . . . .	44	45	89
1880.. . . . .	63	72	135
1881.. . . . .	50	47	97
1882.. . . . .	69	53	122
1883.. . . . .	60	35	95
1884.. . . . .	41	53	94
1885.. . . . .	47	40	87
1886.. . . . .	56	60	116
1887.. . . . .	56	40	96
1888.. . . . .	59	63	122
1889.. . . . .	43	63	106
1890.. . . . .	52	47	99
1891.. . . . .	54	66	120
1892.. . . . .	72	67	139
1893.. . . . .	83	55	138
1894.. . . . .	49	51	100
1895.. . . . .	60	63	123
1896.. . . . .	73	50	123
1897.. . . . .	60	33	93
1898.. . . . .	75	61	136
1899.. . . . .	77	43	120
1900.. . . . .	65	38	103
1901.. . . . .	41	49	90
1902.. . . . .	47	24	71
1903.. . . . .	45	55	100



1904.. . . . .	37	45	82
1905.. . . . .	31	31	62
	<hr/>	<hr/>	<hr/>
	1,509	1,349	2,858

## DEATHS FROM TYPHOID PELLAGRA IN THE ASYLUM.

Years	Men	Women	Total
1901.. . . . .	2	1	3
1902.. . . . .	3	1	4
1903.. . . . .	1	3	4
1904.. . . . .	1	..	1
1905.. . . . .	1	1	2
	<hr/>	<hr/>	<hr/>
	8	6	14

## DISTRICTS OF ORIGIN OF PELLAGROUS INSANE IN THE ASYLUM.

Years	Milan	Lodi	Monza	Gallarate	Abbate-grasso	Total
1901. . .	18	8	13	13	7	59
1902. . .	17	6	12	8	4	47
1903. . .	17	13	15	14	7	66
1904. . .	14	11	15	8	11	59
1905. . .	15	5	10	4	5	39
	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>
	81	43	65	47	34	270
Men.. . . . .						123
Women.. . . . .						147
						<hr/>
						270

Parallel with these yearly statistics of pellagrous insanity we have the report of the cases of ordinary pellagra noted in the province of Milan. According to this, out of 300 communes only 164 are still affected; these are precisely the ones which correspond to the five districts of the origin of the cases of pellagrous insanity, as shown in the table below.

Districts	Total Communes	Pellagra Present
Milan.. . . . .	78	37
Lodi.. . . . .	68	29
Monza.. . . . .	54	47
Gallarate.. . . . .	58	29
Abbiategrosso. . . . .	42	22
	<hr/> 300	<hr/> 164

[In a recent communication on pellagra to his department, Assistant Surgeon Wollenberg, U. S. Public Health and Marine-Hospital Service, reports from Naples, Italy, that:

“Pellagra, despite the extensive interest which is being taken in its suppression, continues to spread in certain regions of Italy. A vigorous campaign has been waged against the disease for a number of years, laws concerning it have been enacted, improvements in grain culture have been encouraged, sanitation has widely improved; the number of pellagrins, however, is diminishing but slowly. The sum which is annually expended for salt, proper food, and hospital accommodations for the care and treatment of the poor affected with pellagra is enormous.

“During the past twenty-five years the extent of

the disease has lessened considerably in the northern part of Italy—Piedmont, Lombardy, Venetia, and Emilia—while there has been a persistent spread in central Italy, very notably in Tuscany, Marches, and Umbria. The disease is now appearing in alarming proportions in Latium and in Abruzzo and Molise, compartments in which it was unknown some years ago. What is most striking is that the disease invaded southern Italy in 1908, cases having occurred in the vicinity of Naples and in Calabria. At present pellagra appears to be firmly established in the lower as well as in the upper portion of the Italian peninsula. The reason for this better showing in the north is not altogether plain, but is partly attributed to the economic, social, and sanitary improvements that have been effected there in recent years.

“In the last triennium the disease was markedly reduced in the provinces of Arezzo, Bologna, Brescia, Florence, Forli, Macerata, Mantua, Modena, Padua, Pavia, Perugia, Pesaro, Rovigo, Treviso, and Venetia. An increase took place in Bergamo, Milan, and Novara. Statistics for central Italy show marked improvement in the province of Perugia. For the rest, the status remains nearly unchanged. In southern Italy there are new cases in the provinces of Avellino and Cosenza. In the same period the total number of new cases reported for the whole country has been gradually reduced as follows:

	New Cases
1906.. . . . .	6,783
1907.. . . . .	5,307
1908.. . . . .	2,766

"The total number of pellagrins in Italy at the present time may be estimated at less than 50,000. Considering that during the years 1906 and 1907 pellagra was the cause of 1,873 deaths and 1,293 cases of insanity, together with the long duration of the illness and its effect on the earning capacity of the afflicted individuals, the above figures are sufficiently startling.

#### TOTAL NUMBER OF PELLAGRINS BY CENSUS.

	Number
1879.. . . . .	97,855
1881.. . . . .	104,067
1899.. . . . .	72,603
1905.. . . . .	55,029
*   *   *   *   *	

"The mortality seems to be lessening. It changed very little after the law\* of 1902 came into effect until the years 1906 and 1907, when there was a fall in the number of total deaths to less than one-fifth of those during the preceding years.

#### TOTAL DEATHS FROM PELLAGRA IN ITALY.

	Number
1898.. . . . .	3,987
1899.. . . . .	3,836

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\*See Appendix No. 1.

1900.. . . . .	3,788
1901.. . . . .	3,054
1902.. . . . .	2,376
1903.. . . . .	2,647
1904.. . . . .	2,363
1905.. . . . .	2,359
1906.. . . . .	439
1907.. . . . .	376

"The hoped-for results and salutary intent of the law—to prevent the consumption of maize of poor quality—have hardly been realized. The law permits the milling of low-grade maize in case it is not to be used as aliment for man, but this provision is held to be difficult to enforce, proper sanitary supervision of country districts being very difficult.

\* \* \* \* \*

NUMBER OF PELLAGRINS IN COMPARTMENTS BY  
CENSUS.

	1881	1889	1905
Piedmont. . . . .	1,328	1,223	1,012
Liguria. . . . .	56	30	56
Lombardy. . . . .	36,630	19,557	15,746
Venetia. . . . .	55,881	39,882	27,781
Emilia. . . . .	7,891	4,617	3,357
Tuscany. . . . .	924	1,125	1,137
Marches. . . . .	406	920	1,436
Umbria. . . . .	872	5,103	4,250
Latium. . . . .	32	146	195
Abruzzo and Molise. . . . .	.....	.....	59

Public Health Reports, July 23, 1909.]

[There are good reasons for believing that Italian statistics on pellagra leave much to be desired in point of accuracy.]

[*Pellagra in Austria*.<sup>1</sup> A correspondent from Vienna under date of July 14, 1908,<sup>2</sup> says: In the eastern parts of the Empire a disease has been very prevalent among the poorer classes for some years past which has proved puzzling to the profession. The clinical symptoms somewhat resembled those of lepra, but differed in not having the anesthetic patches, with consequent dystrophic destructive processes. Profound cachexia with gastrointestinal disturbances are generally observed after the disease has persisted for from 12 to 18 months. In many instances these were the only symptoms, while in other cases circulatory disturbances are a prominent feature. Similar cases were reported from neighboring districts of Russia and Roumania, and many scientists studied the disease. It was finally agreed by the majority of the investigators that the cause of the condition lay in the food. The peasants live largely on maize, making bread and other foods out of this material; a dish called "polenta," consisting of coarsely ground maize with lard, is partaken of heartily daily. In certain wet years the corn was affected by a sporidium and became still more unwholesome because of the presence of certain toxic substances which are held responsible for the disease just described—pellagra. In the province mentioned, inhabited by 1,500,000 people, there are over 38,000 cases reported (3 per cent.).

In the same journal<sup>3</sup> the Vienna correspondent reverts to this subject under date of August 15, 1909:

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<sup>1</sup>The remainder of this Chapter is by the Translators.

<sup>2</sup>Jour. Am. Med. Ass'n., Aug. 1, 1908.

<sup>3</sup>Id. Sept. 4, 1909.

"Since 1905 the action of the government in suppressing pellagra has been going on and including all affected areas. Altogether a population of 2,250,000 has been investigated with the result that about 78,163 persons (3 per cent.) were found to be suffering from one form or another of the disease. Certain districts were more affected than others, and, as a rule, the poorer classes succumbed more easily than those who could procure the food regarded as necessary. The measures of the government have been of a prophylactic nature."

An account of pellagra in Transylvania is given in the *Lancet*, July 16, 1898, p. 164. Transylvania is in the Carpathian mountains, one side being inhabited by Hungarians; the other, by Roumanians—the descendants of Roman legionaries of the time of Trajan and his successors.

When an endemic outbreak was reported from Transylvania a commission was appointed and confirmed the diagnosis of pellagra. But fifteen years previously Dr. Takach reported suspicious cases of skin diseases which he named pellagra, but this diagnosis was questioned by a dermatologist of Budapest. In 1897, however, special orders were issued to hospitals and asylums to be on the lookout for pellagra. Dr. Takach was the first to send in a patient suffering from pellagra. After that numerous cases were found. The disease was thought to be the result of insufficient nourishment, aggravated by bad hygienic conditions and by malaria. No cases could be detected where the people had good and sufficient food. The disease seemed to follow con-

tinuous rains, bad crops and murrain among the flocks.

*Pellagra in Roumania:* As to the prevalence of pellagra in this country it is stated<sup>1</sup> that the staple food of the peasantry is maize, last year's harvest being 126,000,000 bushels. For some reason pellagra has increased. In 1901 there were 33,645 cases; in 1905, 54,689 cases and in 1906 over 100,000 cases. Only three deaths from pellagra were reported in Bucharest, so that the disease is probably confined to the country districts, and may be one of the causes of the high mortality among infants.

*Pellagra in Great Britain:* "Two cases of pellagra have recently been recorded in patients who had never been out of the British Isles, but the published accounts do not tally with the disease as I know it, though the symptoms were somewhat similar to pellagra. One of the patients had never eaten maize but had devoured raw oatmeal and rice."—F. M. Sandwith, Conf. on Pellagra, 1909.

*Pellagra in Jamaica: Strachan's Disease.* In 1888<sup>2</sup> Dr. Henry Strachan, senior medical officer, reported 510 cases of "malarial multiple peripheral neuritis" observed in the Kingston, Jamaica, Public Hospital, full notes having been taken on 121 of these cases.

The patients complained of numbness and burning heat in the palms and soles, often accompanied by cramps, worse at night and in wet weather. Impaired vision and hearing were noted, and a feeling

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<sup>1</sup>*Brit. Med. Jour.*, June 22, 1907, p. 1501.

<sup>2</sup>*Sajous's Annual*, Vol. 1.





of constriction around the lower part of the chest. An eczematous condition appeared on the tops of the eyelids, the angles of the mouth, and the mucocutaneous margins of the nostrils, the lips were unusually red and the palms hot to the touch and hyperemic. Later motor pains of upper and lower extremities appeared. Pain was constant, especially in the feet. Emaciation developed with the progress of the disease. Pigmentation of the palms, soles and lips appeared; respiration is impaired and death may ensue from paralysis of the respiratory muscles. Death is rare, recovery being the rule.

The subjective symptoms are: (1) dimness of vision, (2) impaired hearing, (3) numbness and cramps of the extremities, (4) girdle pain, (5) joint pain, etc.

The objective symptoms include: (1) trophic changes, (2) monoplegias, (3) altered gait, (4) knee jerk was absent in over one-half, exaggerated or subnormal in 23 per cent., normal in rest, (5) cutaneous reflexes varied greatly, (6) sensations were blunted or impaired, (7) soreness of the mucocutaneous lines of junction, (8) wasting of the muscles.

Soreness of the mucocutaneous borders, *i. e.* eyelids, lips, urethra, anus or vulva, was almost the first symptom. Wasting and contraction of the muscles was very marked in extreme cases, the "claw" hand and foot being prominent features. The ophthalmoscope revealed some retinal hyperemia rarely amounting to optic neuritis, but pigmentation of the fundus was observed. Pigmentation of the brain and cord was the only feature observed post mortem. Strachan ascribed the condition to malaria.

Strachan reports further upon this condition.<sup>1</sup> He summarises the condition: (1) Widespread neuritis; (2) Trophic changes in the skin, muco-cutaneous lines and occasionally the cornea; (3) Rare monoplegias; (4) Disease is severe but may last months or years; (5) Recovery is the rule; a fatal termination is rare.

In the last stage when the patient is greatly wasted there may be delusions with feeble attempts at violence. In this condition they may be committed to asylums.

The eyelids are red and irritated. A slightly eczematous condition develops at the corners of the mouth and round the margin of the nostrils, with a fine, branny desquamation. A similar condition appears about the muco-cutaneous line of the prepuce and more rarely about the vulva and anus. The lips and buccal cavity are hyperemic and there may be loss of surface epithelium on the tongue. Palms and soles are hyperemic due to dilated arterioles and later they are deeply pigmented, the color varying from brown to intense black. The gait is typically ataxic. The disease attacks both sexes, youths and adults."

In discussing food poisons, Braddon<sup>2</sup> says: "Another disease probably owning similar etiology is Strachan's Disease, occurring among the natives of the West Indies, which in some respects resembles pellagra. The West Indians live largely, too, on maize."

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<sup>1</sup>Practitioner (London) 1897, LIX, 477-84.

<sup>2</sup>The Cause and Prevention of Beriberi, p. 47.

But, according to Dr. F. M. Sandwith, of London, in a private letter, it is impossible to tell what disease Strachan is describing; certainly not pellagra or beriberi or malarial neuritis. Is it possible that his disease is post dysenteric neuritis, of which there is a good deal in the West Indies? The points against the diagnosis of pellagra are: multiple neuritis, numbness and cramps in hands and feet, dimness of sight, tightness around waist, burning in palms and soles, tenderness over ulnar nerve, patient kept awake at night rubbing feet and legs, atrophy of muscles producing claw hand, facial palsy, deafness, scotoma, patients mostly get well, desquamation of palms and soles, skin eruption confined to muco-cutaneous orifices, palms and soles. Acrodynia might also be considered.

In a recent report (Aug. 21, 1909,) to Surgeon-General Wyman, U. S. P. H. and M.-H. Service, F. van Dyne, American Consul to Jamaica, gives this additional history of this interesting condition:

"In 1897 Dr. Strachan, the late senior medical officer of the Kingston General Hospital, described a form of multiple neuritis met with in Jamaica which he attributed to malarial intoxication, but Sir Patrick Manson, writing on 'beriberi' (Tropical Diseases) does not approve of this diagnosis of the causation of the disease and in a footnote writes as follows: 'Dr. Strachan has described a form of multiple peripheral neuritis which he calls malarial. The disease is endemic and very common in Jamaica. It differs from "beriberi" inasmuch as it is not attended with edema, is frequently attended with implication of the cranial nerves, and is rarely fatal.

We have no account of any similar disease of other tropical countries. Probably, therefore, Dr. Strachan's neuritis is not malarial, but depends on some other cause peculiar, so far as known, to Jamaica. The subject requires further study.'

"Peripheral neuritis due, as it is maintained in Jamaica, to malarial intoxication, is fairly common. The wards of Kingston General Hospital are rarely free from these cases, but it is understood that not a single case of 'beriberi' has been met with in Jamaica. There are medical officers attached to the army here who are familiar with the disease, as it is seen and met with in the East Indies, and they have not found a single case in the Island.

"Pellagra is often met with here, though rarely outside the walls of the asylum, and in last year's annual report the superintendent of the asylum here made the following reference to it:

"'Pellagra is fairly common in our wards. Steps are taken for the eradication of the disease by substituting bread, sugar and fruit for the cornmeal rations. The result is waited for with interest and a definite pronouncement will be made in next year's report. Dr. G. L. Manning, the Medical Superintendent of the Lunatic Asylum, Barbados, has reported similar cases there and he is of opinion the disease is communicable and recommends isolation of all patients.'

"In this year's annual report the superintendent wrote as follows after twelve months' experience of a diet of cornmeal:

"'In continuation of my note in last year's report

on pellagra, a nervous disorder due, it is believed, to the consumption of damaged maize, the attempt made to eradicate the disease by the substitution of bread, sugar and fruit for cornmeal has proved but a partial success. There has been an undoubted diminution of the number of cases in our wards, but as several new cases occurred long after the withdrawal of the cornmeal, I am not satisfied that the condition is entirely due to the consumption of damaged maize, and purpose again restoring, though to a limited extent, cornmeal rations."

Dr. D. J. Williams, Superintendent of the Asylum at Kingston, Jamaica, writes:\* "The existence of pellagra was recognized in our wards about 12 years ago, but as then it was unknown in the West Indies, the correctness of the diagnosis was questioned and the erythematous condition of the exposed limbs attributed to 'sunburn.'

"Four or five years ago the disease was very prevalent in our wards; four per cent. of the inmates—male and female in about equal numbers—were attacked in a population of 1,050. With generous diet, rest in bed and tonics, the majority improved temporarily; others made no improvement, but suffered from chronic diarrhea, progressive weakness and emaciation until death ended the scene."

A corn free dietary, as noted above, was tried for twelve months, but the experiment did not satisfy Dr. Williams that maize is the only cause of this condition. In fact he records his opinion that Indian corn—damaged or otherwise—is not the sole cause of pellagra.

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\*Nat'l. Pellagra Conf. 1909, p. 230.

*Pellagra in Barbados:* Dr. C. G. Manning, medical superintendent of the asylum, Bridgetown, reports<sup>1</sup> that a disease has been prevalent there for about fifteen years which has been termed pellagra by some physicians, but he disagrees and considers the condition "Psilosis Pigmentosa." The chief characteristics are: The patient first declines food and soon refuses it. Examination shows the tongue stripped of epithelium along the tip and edges. The mucous membrane of the jaws and fauces is red and irritated. Soon intractable diarrhea sets in. Dark colored patches appear over the elbows, knees and knuckles. Later the uncovered parts of the feet and hands are affected. The patient rapidly loses flesh and becomes anemic. Mental symptoms appear and commitment to an asylum follows. Under regular diet and treatment improvement follows, but there is a tendency to recurrence. Some patients die of exhaustion.

*Pellagra in Yucatan, Mexico:* Dr. G. F. Gaumer, Izamal, writes:<sup>2</sup> "In 1882 in Yucatan locusts destroyed vegetation, especially Indian corn. Corn being the only cereal used in Yucatan for bread, famine seemed inevitable, until the merchants began to import it from New York. This importation continued till 1891, when the country had recovered from the devastation of the locusts. The imported corn was brought in the holds of vessels as ballast. By reason of exposure to heat and humidity on the voyage, the corn underwent fermentation and

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<sup>1</sup>Trans. Nat'l. Pell. Conf. 1909, p. 232.

<sup>2</sup>Id., p. 233.

became unfit for food. The constant eating of this spoiled corn led to the slow development of pellagra.

"The disease was confined to the lower and middle classes, who were obliged to purchase the cheapest corn in the market. The wealthy class escaped, as they did not eat the imported corn. For the next ten years, 1891 to 1901, Yucatan produced enough corn for home consumption, and cases of pellagra no longer developed. The old cases ran their course fatally. From 1901 to 1907 the corn crops were almost total failures, and corn was again imported in larger amounts than ever before. Mobile and New Orleans were the chief sources of supply, but some came from Vera Cruz—all by water. Again pellagra became epidemic, but was not confined to the middle and lower classes as before. It had been found more profitable to raise hemp than corn, so all classes used the imported cereal. Consequently pellagra spread alike among the rich and poor. At the close of 1907, ten per cent. of the inhabitants were the victims of pellagra, and in August, 1909, not less than eight per cent. of the population had the disease."

*Pellagra in the United States.\** A case of pellagra was reported in 1864, by Dr. John P. Gray, of Utica, N.Y. In the discussion of this case a similar one was cited by Dr. Tyler of Somerville, Mass. Both of these cases were insane. In passing, mention should be made of an epidemic of a pellagra-like condition at the Halifax, Nova Scotia, asylum which was reported by Dr. J. DeWolff as occurring in

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\*See Bibliography for references.



**Plate IV. Egyptian case. Same case as Plate III. Pellagrous "mask."**





1863. It is claimed by Dr. W. J. W. Kerr, of Corsicana, Texas, that pellagra was rife among the Union soldiers at the Andersonville, Ga., prison at about the same time. Dr. H. N. Sloan asserts that pellagra was diagnosed in the South Carolina Asylum at Columbia, in the early 70s, but no written or printed record of it has been found. There seems to be no doubt that the disease existed among the insane patients in this institution in the early 80's, but was not properly diagnosed, being attributed to burns by the sun or fire. Dr. D. S. Pope, of Columbia, is now satisfied that at least two cases of pellagra occurred in the South Carolina penitentiary in the middle 80's.

Dr. S. Sherwell, of Brooklyn, N. Y., reported a case of pellagra in an Italian sailor in 1883. In 1889, Dr. Bemis, of New Orleans, left a written diagnosis of a case in a white woman at the Charity Hospital of that city. In the same year a case of the disease occurred in North Carolina, according to a recent report of E. J. Wood and R. H. Bellamy, of Wilmington. Towards the end of the last century, F. M. Sandwith, of London, having discovered pellagra in Egypt in 1893, and suspecting that it existed unrecognized in the Southern States, corresponded with medical authorities and local physicians in this country, but failed to establish his theory. Later he found an unrecognized case in a recent Italian immigrant in a Boston hospital, where it was classified with cases of cerebro-spinal meningitis then epidemic.

In 1902, Dr. Sherwell reported another case and H. F. Harris, of Atlanta, recorded a case of anchylostomiasis presenting all the typical symptoms of pellagra. In the next few years the diagnosis of pellagra was made in South Carolina, North Carolina and Alabama by at least one general practitioner in each State, but they neglected to place their cases on record. Still, the evidence is conclusive that cases of the disease were recognized. Different asylum physicians in the South Atlantic States now concur in the opinion that pellagra has existed there unrecognized from 10 to 25 or 30 years. Asylum physicians in other States made the tentative diagnosis of pellagra but abandoned it because of the supposed rarity of the disease, or because all the cardinal symptoms were not present in their cases.

An epidemic of pellagra occurred at the Mt. Vernon, Alabama, asylum for negroes in 1906. These cases were studied by Geo. H. Searcy and E. L. McCafferty of the hospital staff, with the assistance of E. D. Bondurant, of Montgomery, and Isadore Dyer, of New Orleans. The outbreak was reported by Geo. H. Searcy in 1907. About December 1, 1907, the diagnosis of pellagra was independently made by the officers of the State Hospital for the Insane at Columbia, S. C., and a careful report rendered to the State Board of Health. This report was given wide circulation.

At about the same time, E. J. Wood, of Wilmington, N. C., had studied a series of cases and reported them in a paper entitled: "A Mixed Infection with

Tertian and Quartan Malaria Occurring in a Patient with Symmetrical Gangrene."

The American disease was identified with Italian pellagra in the summer of 1908, independently by J. J. Watson and J. W. Babcock, of Columbia, S. C., who went to Italy to study the disease. In the spring and summer of 1908 pellagra began to be recognized quite generally through the South.

Following reports made by Passed Assistant Surgeon C. H. Lavinder from Wilmington, N. C., in the fall of 1908, the importance of the disease was at once recognized by Surgeon General Walter Wyman, of the U. S. P. H. and M.-H. Service, who said, "These reports indicate that the disease is more prevalent than has been supposed and that it may in future assume importance from public health and economic standpoints and should receive most careful study."

Special attention was given to pellagra in 1908 by medical organizations in North Carolina, South Carolina and Georgia, as well as other States.

The South Carolina State Board of Health held a conference upon pellagra in October, 1908, and in November, 1909, a National conference on pellagra was held in Columbia under the auspices of the same board. Briefly these are some of the more important steps in the progress of the present interest in this subject in the United States.

Statistics upon pellagra have been unsatisfactory. In June, 1909, a study of the subject claimed that the records showed at least 1,000 cases of pellagra scattered through sixteen States, and a conservative

estimate placed the number at 1,500 cases in the Southern States since 1906. A year later the conclusion was reached that pellagra exists or is suspected in thirty-three States and that the number of cases approximates 3,000 and that a total of 5,000 cases had occurred in the last five years.

Besides at the Alabama and South Carolina Hospitals interesting foci of pellagra have been observed at the insane asylums of Georgia, North Carolina, Florida, Louisiana and Virginia.

In the summer of 1909 the disease was recognized as existing at the Cook County (Dunning) and Bartonville (Peoria) Hospitals in Illinois. In June, 1910, Passed Assistant Surgeon J. D. Long, U. S. P. H. and M.-H. Service, verified the diagnosis in nine cases in the Philadelphia Hospital for the Insane (Blockley).

Several cases have been recognized in the public institutions of California.

Special commissions for the study of pellagra have been appointed by the U. S. P. H. and M.-H. Service and by the Governor of Illinois and the State Board of Health of North Carolina.

*Pellagra in Cuba, Porto Rico and Panama:* Very rarely cases of pellagra have been imported into Cuba from the Asturias and occasionally a tentative diagnosis has been made in natives, or residents, usually alcoholists or sufferers with sprue. (Juan Guiteras.)

B. K. Ashford has reported one case in Porto Rico and J. A. Hayne two cases from the Panama Canal zone.

## GEOGRAPHICAL DISTRIBUTION OF PELLAGRA.

The geographical distribution of pellagra is probably more extensive than is known. This list includes only those places from which the disease has been reported.

## ENDEMIC AND CASES RELATIVELY NUMEROUS.

Northern and Central Italy. Piedmont, Lombardy, Liguria, Venetia, Emilia, Tuscany, Marches, Umbria, Latium, Abbruzzi and Molise.

Roumania. Wallachia, Moldavia.

Austria-Hungary. Tyrol.

Northern Spain. Asturia, Lower Arragon, Burgos, Guadalajara.

Greece. Island of Corfu.

Lower Egypt and Red Sea Coast.

## ENDEMIC AND CASES RELATIVELY FEW.

South Western France. Gironde, Landes, Haut-and Basses Pyrénées, Aude, Haut Garonne.

North Portugal.

Austria-Hungary. Croatia, Dalmatia, Bosnia, Bukovina, Transylvania, Herzegovina, Galicia.

Servia.

Bulgaria.

Turkey.

Greece.

Russia. Bessarabia, Kherson, Poland.

Algeria.

Tunis.

Mexico. Yucatan, Campeche.

South Africa. Kaffirs, Zulus, Robben Island.

United States.

West Indies, Barbados, Jamaica.  
Southern and Insular Italy.

SPORADIC.

Asia Minor.  
India. North Behar.  
South America. Brazil, Argentine.  
New Caledonia.  
West Indies, Cuba, Porto Rico.

DOUBTFUL.

West Indies. Other Islands.  
Central America.

GEOGRAPHICAL DISTRIBUTION OF PELLAGRA IN THE  
UNITED STATES.

ENDEMIC AND CASES RELATIVELY NUMEROUS.

Virginia, North Carolina, South Carolina, Georgia,  
Florida, Alabama, Mississippi, Louisiana,  
Texas, Tennessee, Illinois.

ENDEMIC AND CASES RELATIVELY FEW.

Pennsylvania, Maryland, Kansas, Arkansas, Oklahoma, Kentucky, California.

SPORADIC OR DOUBTFUL.

Massachusetts, Iowa, Ohio, New Mexico, Colorado(?), Missouri, Vermont, Rhode Island, West Virginia, District of Columbia, New York (imported cases), New Jersey (imported cases), Indiana, Wisconsin, Washington, and Michigan.

### CHAPTER III

#### STUDY OF SPOILED CORN—ITS PHYSICAL, CHEMICAL, MICROSCOPIC AND BACTERIOLOGIC CHARACTERISTICS.

One may judge how seriously the Italians themselves regard the eating of spoiled corn by the names given in the different dialects to express its odor—*scagn*, *padul*, *muffito*, *patì*, *sobbolli*, *verdet*, *buttà*, *arbolli*, *smaserido*, *romatico*, *mofflet*, etc.

Spoiled corn may be distinguished on gross examination by its cracked or wrinkled hull, its color of tawny gold, without lustre and with embryo enlarged and blackish; furthermore, it almost always shows external spots, of a brownish color or a greenish color like verdigris, which are due to its diseased condition. If the grain is cut into two symmetrical halves, there is noticed the brownish perisperm and the discolored embryo instead of the normal white appearance. The mass of the perisperm which is around the embryo is often changed into a kind of detritus and in its place there is a cavity in which little *coleoptera* or mites often nest.

The embryo is almost always atrophied, so that it does not fill out its normal place between the perisperm and the hull of the caryopsis. Often the grains have their ordinary appearance, but with eroded points scattered over the surface, and these favor the development of moulds. From this results the greenish blue dust which is found on many grains, a dust which does not remain on the surface but penetrates into the interior. In many grains the



appearance of the moulds and of the *acarus farinae* coincide. The *acarus*, owing to its movements, can be readily discerned with the naked eye.

The meal of spoiled corn is easy to detect by its tawny yellow color, sometimes grayish brown, its slight flavor of mould, its aromatic odor and bitter taste. The merchants make a ready test of spoiled corn meal by rubbing a little in the hand; if the meal is sound the odor of polenta is given off; if damaged, it smells mouldy. [These characteristics, admitting such ready differentiation between sound and spoiled grain belong only to grain decidedly spoiled.]

#### CHEMICAL RESEARCHES ON SPOILED CORN.

If as an experiment grains of spoiled corn, imported in coasting vessels, are digested in 90 per cent. alcohol, their grayish yellow color changes into an intense red; the alcohol itself becomes red, and this color deepens with time. But if grains of sound corn are treated in the same manner they do not change color, even if they remain in the liquid two months, while the alcohol becomes lemon yellow. [This red color was not obtained by Babes and Sion in Roumania, and we have also failed to observe it here except with artificially spoiled corn.]

In a dilute solution of caustic potash the hull of the grain of spoiled corn becomes at first reddish brown; later all the solution becomes brown and gives off a penetrating odor of spoiled corn. The more the decomposition of the corn has advanced, the more quickly the color change takes place. If

this alkaline fluid is neutralized by tartaric acid, flakes of a coffee color are precipitated which have the odor of spoiled corn; these flakes are insoluble in water and ether, but are soluble in alcohol. This same reaction can be obtained with both meal and bread made of spoiled corn. With meal and bread of sound corn the reaction shows a lemon yellow color.

The tincture of spoiled corn yields three substances. The first is, at ordinary temperature, a liquid of ruby red color, with a strong, bitter taste and a very pronounced odor of spoiled corn. It is soluble in alcohol and ether, but insoluble in water, in which it floats; it becomes resinous when exposed to the air, and does not yield a precipitate with the iodide of potassium nor with the chloride of platinum, nor with other metallic salts. With caustic potash and benzine it yields a bright yellow precipitate, and a drop of it on paper makes a greasy spot. This tincture, then, contains the oily substance of corn; it is colored by a red substance which can be isolated from the ethereal solution by caustic potash. Briefly, we shall call this oil the *red oil* of spoiled corn.

The second substance is reddish-brown; styptic and bitter, is soluble in ordinary alcohol, but in absolute alcohol it precipitates yellowish flakes, which dissolve quickly if a little distilled water is added. It is also insoluble in ether and yields, when treated with iodide of potassium, a flaky precipitate; with chloride of platinum it yields likewise a flaky precipitate of yellowish color; with sulphate of copper

it becomes green; at the end of a certain time a reduction of protoxide takes place; it is soluble in acetic acid and a solution of caustic potash, from which it can be precipitated by means of sulphuric acid; treated with much water it separates into two parts, one of which, insoluble, is precipitated in the form of a brown amorphous powder; the other makes a bright yellow solution. This is *pellagrosine* or the *toxic substance* of spoiled corn; and, as we shall see, its toxicity is very marked.

The third substance, when heated with ether, solidifies into a mass which becomes hard on exposure to the air. It is soluble in diluted alcohol and in a solution of caustic potash; in water, absolute alcohol and benzine it is insoluble. When heated it becomes semi-solid and can be drawn out in threads like sealing wax; it burns with a white flame giving off the odor of burnt polenta; this is the *resinous substance of spoiled corn*.

The tincture of sound corn yields likewise three substances. The one is not red, but is of a beautiful yellow amber color, is soluble in ether and has not the strong odor of the *red oil of spoiled corn*; it is not, like the red, precipitated when treated with benzine, does not become resinous when exposed to the air; in short, it has all the properties of normal commercial oil of corn. The second is, likewise, yellow, does not yield a flaky precipitate with iodide of potassium nor with absolute alcohol, but with caustic potash and sulphuric acid yields a precipitate soluble in ether. The third resembles the *resinous substance of spoiled corn*.

In passing, it is worth noting that the substances isolated from spoiled corn are chemically analogous to those isolated from spurred rye (ergot); and the toxic substances of spoiled corn, if given in small doses for a long time, will show physiologic and therapeutic activity similar to those of ergot administered in the same way.

### DIFFERENTIAL CHEMICAL REACTIONS OF

#### *Spoiled Corn*

Is colored red in alcohol and caustic potash.

Yields with alcohol a red tint.

Yields an oil, bitter, ruby red, which is dissolved in alcohol, gives a precipitate with benzine, becomes resinous when exposed to air, contains a pigment which can be isolated by caustic potash from an ethereal solution.

Yields a red substance, slightly poisonous, which, when dissolved in caustic potash and sulphuric acid, produces red-brown flakes, insoluble in ether. Precipitates in iodide of potassium reddish flakes, in absolute alcohol flakes of a pale yellow color.

The name Toxic Substance of Spoiled Corn (Pellagrosine) is given to this body.

#### *Sound Corn*

Does not change color in alcohol or in caustic potash.

Yields with alcohol a lemon-yellow tint.

Yields an oil of yellow amber color, without odor, insoluble in alcohol; does not become resinous when exposed to the air; does not yield a precipitate with benzine, but dissolves at once.

Yields a yellow substance, which does not precipitate either with absolute alcohol or iodide of potassium; this product becomes liquid in sulphuric acid and ether and is absolutely harmless.

The chemist Erba perfected the method of extracting these substances. He placed large quantities of sound corn in casks, filled about one-third full of water. These were shaken daily so that all the grain came into contact with the water. Daily examinations were made. The grain passed slowly through acetic, alcoholic, lactic and putrid fermentations. At this stage it was dried. The grain was then seen to preserve its usual form, but had assumed a dark, dirty, yellow color, while the embryos were of an intense yellow and richer than normal in oil. The starchy part of the grain appeared grayish white. The corn to the touch was less compact and was easily pulverized. The microscope revealed an abundant growth of several moulds, including principally *aspergilli*, *eurotium herbariorum* and *oidium lactis*.

The corn was next dried till it lost 24 per cent. of its weight, ground, and the meal treated with 40 per cent. alcohol to extract soluble substances. Distilling this tincture on a water bath, and treating the residue, there were obtained an oily substance designated as the *oleoresin of spoiled corn* analagous to the *red oil* mentioned above; a substance identical with the *alcoholic extract* or *pellagrosine*; a resinoid substance designated as the *glutinous substance of spoiled corn*; and a substance designated as the *aqueous extract of spoiled corn*.

The embryos of spoiled corn, treated in a similar manner, yielded only an oil, or rather fat, which remained solid even at 19° C.; and the *alcoholic extract* in small quantity.

Corn bread (*pane giallo*), moulded and spoiled up to the lactic fermentation stage and exposed to moist heat, under treatment, yielded a greater quantity of fat of a yellow color and aromatic odor, which remained solid at 19° C. Large quantities of sound corn, submitted to the same methods, yielded a very small quantity of oil and almost none of the alcoholic extract.

From artificially spoiled corn there was obtained, from 15 liters of tincture (prepared from 100 kilos of corn) 3 kilos of *oleoresin* and 800 grams of *pellagrosine*.

Submitted to analysis by Brugnatelli the oil and the alcoholic extract from spoiled corn showed the presence of a bitter, nitrogenous body, which gave the reactions of an alkaloid resembling strychnine. This alkaloidal body was not found in the sound corn.

#### MICRO-ORGANISMS OF SPOILED CORN.

We shall omit the discussion of *Sclerotium maidis*, analagous to the fungus of mildew of rye and barley, which is found only in Colombia, where it causes in animals falling of the hair, the teeth, the nails and paralysis of the lower extremities (Roulin), but not pellagra. Nor shall we speak of the smuts *Ustilago maidis* and *Uredo carbo*, because grain so affected is not used, and therefore cannot have any direct connection with pellagra.

There remain to be considered:

1. *Sporisorium maidis*. This is the best known parasite of spoiled corn. The study of pellagra in

Italy began a new era with its description; it is of a greenish color and is observed in the furrow of the embryo, and, as seen under the microscope, resembles little globules united by fine filaments, but separable by rubbing.

Balardini, who, with Cesati, was the first to describe this hyphomycete, experimented with it on man, and produced gastritis and diarrhea; with chickens it caused loss of feathers, decided loss of weight and droopiness.

With regard to the etiology of pellagra, however, this micro-organism has no importance, for Lombroso found only three specimens of it in Lombardy during many years.

Balardini has not been able to find it again, even during rainy seasons. If an organism is responsible for a disease so widely spread as pellagra, it would itself be more widely distributed instead of being a curiosity.

2. *Penicillium*. In all the spoiled grains a quantity of *Penicillium glaucum* is found, which exhibits perpendicular filaments, from which are developed in great number flaky, easily scattered conidia. They compose the greenish-blue dust which is found on most of the grains of spoiled corn. This does not remain on the surface, but penetrates into the interior, principally in corn placed on the ground level in the winter, or during fermentation in damp granaries.

3. *Oidium lactis maidis* is composed of simple, spore-bearing, straight and colorless filaments, and a terminal chain composed of short, cylindrical

spores of 0.0077 up to 0.0108 mm. in size. It develops at 19 degrees C., and the corn develops first alcoholic and later butyric fermentations.

4. *Eurotium herbariorum* is found in the damp corn imported by coasting vessels from the Danube.

5. *Aspergillus glaucus* is found in the same conditions as *Penicillium*, but more rarely.

6. *Sporothrichum maidis* was found in 1873 by Professor Garovaglio on corn which had been exposed to storms. It was a new hyphomycete of the genus *Sporothrichum*, and is very rare.\*

With ordinary meal of spoiled corn one may obtain by cultural methods these micro-organisms:

1. A very small, cylindrical bacillus, very motile, which multiplies by fission, 1 to 3 micra in length,  $\frac{1}{2}$  micron in width, which grows in chains of two or three elements; stains readily with an alcoholic solution of methyl violet and with the usual aniline dyes as well as with dilute hematoxylin; it resists a temperature of 90 degrees and grows luxuriantly at 25 and 30 degrees C. This is the *bacterium maidis* or, better, *mesentericus vulgaris* (potato bacillus).

2. Frequently another very small, short bacillus sometimes growing in chains, which stains well with the aniline colors—a variety of *bacterium thermo*, sometimes found in organic matter undergoing putrefactive changes.

3. In many specimens of spoiled meal, or in bread made from it, is also found the true *bacterium thermo*, 1.5 micron in length, 0.5 to 0.8 micron in width.

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\**Rendiconti del R. Istituto Lombardo*, 1873.



4. In other specimens there is found the *bacillus tremulus* 3 to 7 micra in length, 0.4 micron in width, but its presence is not characteristic.

5. Diplococci are found in small numbers, and numerous colonies of small micrococci which are equally common in putrifying substances and in good corn bread.

It is to be noted that in many specimens of meal only the *bacterium maidis* is found, while at other times this organism appears in cultures along with many other organisms.

Breads made of thoroughly tested meal were examined microscopically soon after leaving the oven. The potato bacillus was found in great numbers. This bread, after being broken open, was placed in a damp chamber; at the end of eight or ten days it showed numerous yellowish and bluish spots, which, according to the examination of Professors Mattiolo and Gibelli were composed of the following micro-organisms:

1. *Rhizopus nigricans* (Ehrenberg).
2. *Mucor Stolonifer* (De Barry).
3. *Eurotium aspergillus glaucus* (De Barry).
4. *Aspergillus glaucus* (Linck) with many mature conidia.
5. *Bacterium maidis*.
6. Conidia which came probably from *Oöspora verticilloides* (Saccardi).
7. Abundant mycelia, coming probably from a *Pyronomycete* (an absolute certainty is impossible, because pure cultures were not made); very likely from *Oöspora verticilloides*.



Plate V. Egyptian case. Hands of case shown in Plate III. Skin much thickened. Dermatitis dry and scaling.



It is worthy of remark that the *bacterium maidis* was also found in sound meal and in the bread made from this meal. The bread after analysis was given to dogs, and the results will be found further on.

Cuboni found in spoiled corn and meal *saccharomyces mycoderma*, and once a profuse development of *sarcina ventriculi*; he found *Oöspora verticilloides* on corn which had remained on damp ground, but never on corn imported by coasting vessels. But he devoted most of his attention to the *bacterium maidis*.

In 1881, Majocchi found a very motile bacterium in both sound and spoiled corn, but always in greater numbers on spoiled corn—this micro-organism he called *bacterium maidis*, and he thought he found it also in the blood of seven pellagrins in the first stage of the disease. Cuboni, working with this micro-organism, found it constantly and abundantly on spoiled corn. He also called it *bacterium maidis* and recognized its similarity to the *bacterium thermo*, though it resisted a higher temperature.

With corn very much spoiled by sea-water, this bacterium can very easily be recovered from the interior of the grain.

This bacterium is not injured by a warm solution of chloride of sodium, or of sulphate of calcium, but is killed by arsenite of sodium in the proportion of .03 gram to 250 grams of polenta and by 0.5 gram sulphate of quinine to 200 grams.

According to Cuboni, the development of the *bacterium maidis* occurs in damp corn, and more readily still in immature corn. Dryness arrests its develop-



ment absolutely, but without destroying it. This is why corn well dried can spoil if it again becomes damp. This bacterium resists a temperature of 98 to 100 degrees C., so that, even during the cooking of polenta, some bacteria survive. Cultures on gelatine show white points on the surface which spread slowly and liquify the medium. In a tube the cultures assume the funnel shape.

Comparing the feces of healthy individuals with those of pellagrins, Cuboni arrived at the conclusion that the latter harbor much greater numbers of this bacterium; when introduced by spoiled polenta they multiply enormously and occasion a true intestinal mycosis.

Paltauf and Heider have likewise studied the peculiarities of the bacterium *maidis*. They give its length as 2-3 micra, very rarely 4-5 micra; its smaller forms are rounded at the ends and are very motile; sometimes they form long chains. It is colored by the usual aniline dyes, but especially by methylene blue. It is an aerobe which grows well at ordinary temperatures. Spores are found in the middle or at one extremity and occasionally free in old cultures. In from 24 to 36 hours, gelatine plate cultures show superficial, circular colonies with irregular edges and there occurs a funnel-shaped liquifaction of the medium. Cultures on potatoes show a granular and wrinkled membrane. On agar and also in blood serum a very fine membrane appears which covers the entire surface; on corn meal it forms a grayish-white membrane, which later becomes brown and slowly liquifies.

From all these peculiarities, they conclude that it is the potato bacillus. Paltauf searched for it in the feces of pellagrins and found it in fifteen patients, but its presence in the intestines of the pellagrous does not seem pathogenic.

Heider, working in the laboratory of Professor Ludwig, at Vienna, studied the biology of *bacterium maidis* and its chemical products. According to these studies the bacillus is a strict aerobe, grows well in alkaline media, but will survive in neutral or even slightly acid media. Albumenoid media are broken up by this organism with the production of ammoniacal substances, traces of sulphur and an amine, probably the trimethylamine; indol, skatol and phenol are absent. Starchy substances are converted into sugars, and from saccharine solution is produced a volatile body allied to the aldehydes or ketones, also acetic, butyric and perhaps a small quantity of succinic acids are formed. Milk is acidified and coagulated. These observations indicate that at a high temperature and with a certain humidity this bacillus can promptly produce changes in corn.

Bordoni-Uffreduzzi and Ottolenghi have found that in polenta this bacillus resists an energetic sterilization. It is only after repeated sterilizations, under high pressure, that it ceases to develop. Polenta sterilized, infected with the potato bacillus and placed in the thermostat, becomes covered with a very thin membrane, ashy gray in color and with light folds, which thickens and at the end of five days becomes spongy in character. Later liquified

spots make their appearance and spread slowly over the whole surface; at the end of 20 or 30 days the polenta becomes of a thick, soup-like consistency with a dark *café-au-lait* color. Kept for some months at the same temperature, no further changes occurred. On the third day the culture develops a strong mouse-like odor.

We shall return to the experimental results of feeding dogs with corn infected by this bacillus.

Monti and Tirelli made new and very accurate studies of spoiled corn in the laboratory of Golgi. From time to time they ground their corn afresh under antiseptic precautions and used the plate culture method of Koch and Esmarch.

They found fourteen different micro-organisms. The most numerous were the *Penicillium glaucum*, *Eurotium herbariorum*, *Mucor racemosus*, *Oöspora verticilloides* and *Bacterium mesentericum vulgare* (potato bacillus) and *Rhizopus nigricans*,—none is directly injurious to the human organism, but all are notoriously capable of decomposing the cereals upon which they vegetate. Monti says: "It is easy to understand that *Mucor racemosus* and *Rhizopus nigricans* are important in the fermentative processes of corn."

The presence of the saccharomycetes is explained by the great percentage of starchy substances contained in corn, but the presence of the putrefactive bacteria, like the *bacterium thermo*, indicates that in spoiled corn, besides fermentative processes, putrefactive changes also play a part.

From another point of view, the presence of micro-

organisms which are also found in water, shows that the corn is damp from rains, dews or dirt, and this justifies the ancient custom requiring that corn be dried under cover. It is more than probable that in consequence of the drying, many of the organisms die, and even the most resistant no longer find a favorable medium for development.

[The moulds found on spoiled corn are very numerous and a great deal of study has been given to their relative importance on spoiled corn. Tiraboschi, under Gosio's direction,\* has devoted much time to this subject. From an examination of 432 specimens of spoiled corn obtained from places where pellagra was endemic and serious, he reported, at the end of two years' labor, the following moulds, named in the order of their frequency: *Penicillium glaucum* (Link), *Oöspora verticilloides* (Sacc.) (Tirab.), *Aspergillus niger* (v. Tiegh), *Aspergillus flavus* (Link), *Aspergillus varians* (Wehmer), *Aspergillus fumigatus* (Fres.), *Aspergillus ochraceus* (Wilh.), *Aspergillus effusus* (Tirab.), *Aspergillus glaucus* (Link).

These studies, Gosio remarks, confirmed the great preponderance of *Penicillium glaucum* over other moulds, but the low temperature at which this mould will develop has naturally resulted in its greater prevalence, and has, therefore, possibly given it a position of false importance.

These moulds, as Tiraboschi states, are limited to three genera: *Penicillium*, *Aspergillus*, *Oöspora*,

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\*B. Gosio. Sul problema etiologico della pellagra—Atti del Terzo Congresso Pellagrologico Italiano, 1907.





In a more recent paper (1908) Tiraboschi has commented on the varied flora of spoiled corn, and pointed out the importance of the regions from which such corn may have originated. And he describes three new moulds found by him on imported, spoiled corn, which had never been reported as found on spoiled corn previously, namely, *Oöspora aegeritoides* (Karst), *Harmodendron cladosporiodes* (Fres.) (Sacc.) and *Diplodia maidis* (Berk.) (Sacc.)]

## CHAPTER IV

### EXPERIMENTAL RESEARCHES AND ETIOLOGY.

Although very probably the cause of pellagra is to be found in the chemical and molecular changes which take place in corn under the influence of numerous micro-organisms, practically innocuous in themselves, which vegetate on this grain, yet it is difficult to find the remote and indirect cause of the malady [that is, the particular parasite or parasites responsible for the production of the specific toxins]. It is useless to delay over the question of the harmlessness of the very frequent *Penicillium*. The administration to three persons of half a grain of spores of *Penicillium glaucum* from corn produced no other result than a metallic taste and burning in the pharynx. A subcutaneous injection of .02 gram gave only a local inflammatory reaction. Two rats fed for 20 days on this same mould, taken from corn bread, lost weight but presented no pellagrous symptoms. Grohe showed that spores of *Penicillium* and *Aspergilli* injected intravenously in dogs gave no toxic symptoms. According to Carlo Ceni, the *Penicillia*, however, have a direct poisonous action. [Ceni's work will be discussed elsewhere.] But according to Monti, the *Aspergilli* in symbiosis with other micro-organisms must be charged with setting toxalbumins free.

Tizzoni, on the other hand, considers only the microbic action and undertakes the task of demonstrating that in the grave and rapidly fatal forms of pellagra, a constant specific micro-organism is found,

whose characteristics he has described and which he has been able to cultivate. He finds it in the blood, spinal fluid and organs at death.\* [Some discussion of Tizzoni's work will be found elsewhere.] This could be, however, a secondary infection.

*Oidium Lactis*.—The harmlessness of *Oidium lactis* is today recognized. However, it always accompanies that advanced fermentation of corn in which occur those substances which produce convulsive phenomena, as experiments in the laboratory have demonstrated (Erba and Lombroso.) The fermentation of corn by the *Oidium lactis* gives rise to substances which produce a syndrome, having much analogy with the paralytic and convulsive forms of pellagra, as is shown by the experiments of Ottolenghi and Lombroso.

Cultures in broth of *Oidium lactis* were scattered over the surface of sterilized polenta, which was kept in a moist chamber; this polenta was kept six days at 37 degrees. Grayish white spots developed on the surface, slightly opaque, glistening and having the appearance of colonies of *Oidium lactis*. The seventh day, in the laboratory of Professor Giacosa, an extract of one kilogram of this polenta was made with 1,750 grams of distilled alcohol; the alcohol was rectified by distilling with tartaric acid; the polenta in a suitable apparatus was put to boil in the alcohol for twelve hours; from this the larger part of the alcohol was separated by filtration, the rest was put on a water bath and filtered from time to time to separate the deposit. There finally remained a liquid, chestnut brown mass of .70 grams, of which 1 gram represented 14.28 grams of polenta. This material was used in ten experiments by subcutaneous injections on frogs, guinea pigs and rabbits.

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\**Reale Accademia dei Lincei, OOOIII, 1906.*

The lethal dose of this extract was found to be in the case of the frog, 14 grams of the extract to the kilogram of animal weight; with the guinea pig 18; with the rabbit 33. In the case of four frogs, three guinea pigs and one rabbit, death occurred with sensory-motor paralysis; the animals which survived exhibited paralytic phenomena which later slowly disappeared. Tonic cramps were observed in four frogs; two died in opisthotonos which persisted even after cadaveric rigidity. Upon dissection, was found: premature cadaveric rigidity in three frogs and retarded in one rabbit; arrest of the heart in diastole in three guinea pigs and in systole in three frogs which had presented tetanic phenomena. In two frogs there were ecchymoses in the muscles. In two others there were bloody infiltrations in the cellular tissues of the abdomen at the site of the injections; in two frogs and in one guinea pig there was effusion of blood in the abdominal cavity.

### BACTERIUM MAIDIS.

Numerous experiments have been made with cultures of the *Bacterium maidis* of polenta. This micro-organism has occupied much of the attention of the students of pellagra. However, its identity with the potato bacillus, and the fact that it does not predominate in the stools of pellagrins ought to have led to this conclusion: that its action is indirect only and is similar to that of *Oidium Lactis* in that it produces from the parenchyma of the grain toxic substances.

Paltauf made subcutaneous injections in rats, guinea pigs and rabbits of young and old gelatine cultures of this bacillus and he found that it produced results in only one rat which was found ill from cysticercus.

After this negative result he made an attempt with the alcoholic extract of corn meal, infected with this bacillus and left three months at a temperature of 35 degrees. He injected this extract into white mice in doses of 0.5 c. c. These animals showed coma and paralysis with death, at the end of two hours. In frogs the injection of 1 c. c. produced a state of temporary feebleness. The cultures of the potato bacillus in polenta and their extracts gave the same results.

The identity of *bacillus maidis* and the potato bacillus seems, therefore, proven. Heider, with Gorizia, has also extracted a substance from spoiled corn which gives the reaction of an alkaloid and which killed rats with anesthetic and narcotic phenomena.

These experiments were repeated on a larger scale by Lombroso, Ottolenghi, Bordoni-Uffreduzzi, and their results are given below:

If cultures on polenta of one, two, six and up to seven days old, are given to animals they become accustomed to it slowly; the initial diarrhea, which is the only symptom, may even cease; the cultures over four to five days old are refused, perhaps because of their bad and very pronounced taste.

As a consequence of this nourishment, digestive troubles are produced, sometimes vomiting, almost always diarrhea, but never derangement of the sensibility or of the motor system. At the end of some days the weight begins to diminish, but then maintains itself within normal limits. The temperature is usually maintained at normal; in the first days only two cases showed a slight evening rise.

The attempt to cultivate this bacillus on wheat bread met

with little success; two dogs fed for fourteen days with this bread showed no change.

An experiment was then made with the alcoholic extract obtained from a culture on polenta twenty-five days old. The extract, prepared by Professor Filletl, was injected into three dogs under the skin of the back in doses of 5%, 10% and 25% of the weight of the animal. The two dogs which had received the largest doses died two days later, after presenting the following symptoms:

Paresis of the hind legs, almost continual tremor, general depression, which was rapid and progressive, gradual loss of voluntary motion, complete paralysis of the hind legs, mydriasis, slight increase of temperature, acceleration of respiration and pulse, insensibility, bloody diarrhea and death with prolonged agonistic state. At the autopsy, edema of a hemorrhagic nature in the hypogastric region, extravasations in the spleen.

The dog inoculated in the proportion of 5 per cent. of its weight exhibited at the beginning the same symptoms, but at the end of the second day his condition improved; however, the hind legs remained paralyzed and the diarrhea continued for several weeks with a remarkable diminution of weight.

In the case of two other dogs, intravenous injections, in the proportion of 5 per cent. of body weight caused death after the development of the above mentioned symptoms.

Injections into ten frogs, with corresponding doses, brought on death in three hours with paralysis, diffuse ecchymoses on the interior of the thighs and in the hypogastric region. Intravenous injections of the extract of sound polenta up to 10 per cent. had no evil consequences; the same may be said of the subcutaneous injections made in double doses.

The *bacterium maidis* is, therefore, inoffensive *per se*, but releases from corn a ptomaine that has a toxic action, eminently paralyzing.

*In pellagra, then, we are dealing with an intoxication produced by poisons developed in spoiled corn through the action of certain micro-organisms in themselves harmless to man.* [This expresses succinctly Lombroso's theory of the cause of pellagra.]

Since 1883 Lombroso and Peschel have done experimental work upon the toxicity of the blood of pellagrins as compared with the toxicity of cultures of *bacterium maidis*.

This bacterium is active in decomposing the albumenoid substances and hydrocarbons of corn into toxic substances; perhaps it acts also in an irritating manner on the digestive tract.

The *bacterium maidis* does not multiply merely in the grains and meal of spoiled corn, but also in sound corn and in the normal intestine (*Bacillus mesentericus vulgaris*).

It is not found in cultures made from the blood of grave cases of pellagra. Cuboni sought for it in vain in thirty cases of pellagra. Even in the erythematous skin and in the viscera of pellagrous dogs nothing is found; or, if from their cadavers a growth is obtained it is due to putrefactive bacteria. When the blood or urine is drawn antiseptically and planted, such cultures remain sterile. On the other hand, symptoms of pellagra appeared in animals that had fed upon the alcoholic extract or the tincture of spoiled corn, from the preparation of which every microbic element was excluded.

The injections of cultures of *bacterium maidis* grown on sterilized blood serum, and the injection of a culture made from the blood of typhoid pel-

lagra produced only the febrile disturbances due to the pyrogenous substances commonly found in almost all such cultures. As often as these experiments were repeated, the animals on no occasion developed symptoms of pellagra, nor of rapid diminution of weight, nor of rapid increase of temperature; and never any of the cutaneous, muscular and nervous symptoms which were met with in dogs fed with spoiled corn.

Some authorities have attributed these febrile phenomena to the influence of special micro-organisms. They have taken these toxic manifestations for pellagrous phenomena; and probably having obtained, with poor technique, a positive result in their cultures, have erroneously concluded that the animal was suffering from a true infection.

But all the pathology of the disease protests against any parasitic hypothesis; it is not transmissible by contact and has the greatest analogy with alcoholism, which certainly cannot be suspected of having a microbic origin.

Moreover, pellagra does not declare itself because one may have eaten once or several times of spoiled corn; it is necessary to continue the eating of it during a certain length of time in order that the poison may have its effect. In the case of dogs under experiment it was necessary to wait six or seven days, often several months, in order to see the first true pellagrous manifestations appear. It is for this reason that the people of the country and the physicians, with some exceptions, have found difficulty in believing that the disease could come from eating spoiled corn:



Nor is there any other parasitic disease, in which an amelioration is produced as soon as poor nourishment is replaced by wholesome food without any change in the other conditions of existence. Something analogous is seen in the undoubted cases of slow poisoning seen in alcoholism, and in the hydrargyrisms of laborers in mercury mines; there the symptoms of the disease disappear as soon as the introduction of the poison ceases. Infectious diseases have, besides, a progressive course, are rarely intermittent, and are not arrested when the diet is changed. Very many of them also show a great increase of temperature and have a much more pronounced tendency to localize themselves in an organ or a tissue, which is not the case in pellagra.

#### GRAIN AND MEAL OF SPOILED CORN; AND MOULDY CORN BREAD.

When in 1883 the corn harvest was spoiled by hail and inundation in the districts of Mazzè and of Vischi, some of it was bought where it was grown. It was submitted to botanical examination by Professors Gibelli and Mattiolo. The grains were found spoiled by the *Aspergillus* and by the *Rhizopus*, to some extent also by mites and the *Bacterium maidis*. With this corn and other foods such as milk, flour-bread, scraps of meat, bone (to prevent the objection of inanition), ten dogs were fed for from six or eight weeks up to end of life, and a larger number of chickens. Here is a résumé of this series of experiments:

**WEIGHT.** In the case of all dogs undergoing the experiments the weight diminished except in one (a young dog which had not attained its full growth). In the other cases the diminution commenced at the end of three, four, five, six, seven and twelve days. It cannot be said that the diminution was due to the exclusive use of the corn, for it was less in those which for a time received the corn only, and it was more pronounced in those in which milk, white bread and bones were given at the same time.

**TEMPERATURE.** Almost always an elevation of temperature showed itself coincident with the diminution of weight—a circumstance that demonstrates almost with certainty that during the experiment a toxic pyrogenetic substance was introduced, analogous to that of the infectious diseases. The development of the temperature is a sign still more characteristic than the diminution of weight, for, during seven months, the weight of the youngest dog increased, while the temperature was constantly elevated. In pellagra, therefore, it is not a question of a state of inanition, for in this case there would have been diminished temperature. Elevation of temperature is not in most cases the result of the reduction of the substance of the body, but of poisons introduced into the organism. Inanition does not come into play, for there is often a parallel increase in weight. The elevation of the temperature, the appearance of tetanic and spastic symptoms, and the frequent appearance of anemia (symptoms not peculiar to inanition) prove it abundantly.

**PULSE AND RESPIRATION.** The pulse and the respiration did not show digressions, save in two cases (dogs), in which tetanic movements showed themselves and, at the same time, sudden interruptions of the respiratory rate, with extreme acceleration.

**ANEMIA.** Reduction in red blood cells often shows the anemia of the pellagrous, but this anemia it not constant. This fact demonstrates that nourishment by spoiled corn does not cause chronic inanition, for this produces constantly a decrease of red cells. On the contrary, two dogs to which bread or broth of moulded corn was always given, showed

an increase of red cells. In one case of sudden death with tetanic phenomena, there was no appreciable reduction.

**MUSCULAR SPASMS.** A symptom, frequent, but not constant, is the tonic muscular spasm, and the increase of the tendon reflexes (with two dogs the tetanic state was very pronounced). These cases would appear in their true aspect in the light of experiments with the alkaloidal substances and with the oil of spoiled corn. The inconstancy of the phenomenon is therefore admitted. (In seven cases out of ten a complete torpor of the muscles was produced; in six cases a cerebral torpor; in three, loss of sensibility; in four cases out of ten muscular tremors).

**DIARRHEA.** The most frequent of the complications was diarrhea, which was often preceded by refusal of food and dysphagia (seven cases), the latter symptom being most often due to muscular spasm, and manifested so much more frequently than in human pellagra as to make it a special characteristic of canine pellagra.

**THE SKIN.** The erythema of the skin was manifested only once, completely and certainly, and then in a dog which remained free from anemia, torpor and spasmodic phenomena, and in which the sitophobia and paresis disappeared with the appearance of the erythema. The microscopic examination of the skin in this case did not, however, exclude all idea of a parasitic cause, and threw some light on the origin of the erythema by showing proliferation of the cellular nuclei and infiltration by plasma cells in the deep layers of the skin.

To sum up, we can say that in dogs pellagra shows itself sometimes under the anemic form, sometimes under the spasmodic form and sometimes under the cerebral form, which is precisely analogous to the pathologic anatomy and symptomatology of pellagra in man, in whom it is erroneous to speak of pellagra in general, and is more didactic than scientific to make divisions into first and second stages. A more



**Plate VI. Italian case. Symmetrical, dry, scaly dermatitis of hands and forearms. Characteristic facial expression. Courtesy of W. Bayard Cutting, Jr.**



accurate division would be into anemic, spastic, tabetic, cerebral, and other similar forms of pellagra.

Nutrition with bread from moulded corn calls forth the same symptoms as nutrition with the grain or meal of moulded corn. If it never causes true tetanic phenomena, it is, however, accompanied by rigidity of the lower extremities, with exaggeration of the tendon reflexes—symptoms more characteristic of pellagra. Later cutaneous erythema, the most typical symptom of pellagra, shows itself distinctly. This was lacking in other experimental animals, although it is known to occur in "*enmaizados*" horses in Mexico, in which it is notable that stupidity and dysphagia appear shortly before the erythema, and disappear with its advent. And this is in wonderful accord with the observations of medical practice which tend to establish an antagonism between the nervous phenomena and the skin symptoms. Perhaps localized hyperemia acts as a cutaneous revulsion—one sees nervous diseases modified by the employment of a strong irritation of the skin. In general the symptoms are more benign in animals fed on mouldy bread.

In twelve chickens fed on spoiled corn convulsive phenomena were exceptionally noted, and if a complete marasmus could be excluded, the spoiled grain alone produced increase of weight, but finally death intervened after atrophy of the feather follicles, with changes in the skin and horny appendages. A fact worthy of remark is that chickens entirely tame for months became very wild at the end of five or six months on the regimen of corn; they fought their

companions and had to be shut up. Another chicken had photophobia and was unwilling to leave the cage.

Taken altogether, the disease was less pronounced in the chickens than in the dogs; however, the chief effects of nourishment with spoiled corn, especially the cutaneous symptoms and muscular disorders, showed results analogous to those of the subcutaneous injections of extracts of oil and of other preparations of spoiled corn.

#### TINCTURE OF SPOILED CORN.

The proof seems, then, to be regarded as established, that in pellagra the chronic poisoning does not come from microbes infecting the animal organism, but from the chemical transformations of the parenchyma of corn; and since the more important toxic substances pass into the tincture made from the grain, it would seem wise and profitable to study experimentally the action of this tincture. This would seem all the better since the tincture is very well adapted for administration to human beings.

The tincture of corn spoiled by *Penicillium glaucum* was given, for a length of time, to twelve sound and healthy individuals, soldiers and laborers at work in the city, and, at the time of the experiment, well fed. Results are given below :

Symptoms.	Number of Cases.
Bulimia.. . . . .	9
Pruritus of back and face.. . . . .	8
Loss of weight.. . . . .	8

Urine diminished and of high specific gravity.. . . .	8
Diarrhea.. . . .	6
Diurnal somnolence.. . . .	5
Eructations.. . . .	5
Persistent muscular weakness.. . . .	5
Desquamations.. . . .	5
Headaches.. . . .	4
Anorexia.. . . .	3
Burning of the eyelids.. . . .	3
Repugnance for water.. . . .	3
Hyperidrosis.. . . .	3
Ephelides on the arms and hands.. . . .	3
Palpitation of the heart.. . . .	3
Syncope.. . . .	3
Variations in the pulse.. . . .	3
Increase in weight.. . . .	2
Intense thirst.. . . .	2
Increase of muscular force.. . . .	2
Sensation of heat in head.. . . .	2
Sensation of warm water on back.. . . .	2
Irritability and emotionalism.. . . .	2
Restlessness at night.. . . .	2
Erythemas.. . . .	2
Tinnitus aurium.. . . .	2
Redness and burning of the skin.. . . .	2
Burning of scrotum.. . . .	1
Mydriasis.. . . .	1
Ptoxis.. . . .	1
Prickling sensation.. . . .	1
Oppression and precordial pains.. . . .	1
Vertigo.. . . .	1
Furunculosis.. . . .	1
Enteralgia.. . . .	1
Sensation of foreign body in head.. . . .	1
Salty taste.. . . .	1
Burning in the throat.. . . .	1
No symptoms.. . . .	2





It is worthy of remark that though the experiments were made on a small number of persons, varied symptoms were manifested; in some cases heart symptoms developed; in others skin or nervous symptoms; sometimes the symptoms developed late, sometimes with astonishing rapidity; some presented no symptoms at all.

At any rate, the proof of the harmfulness of spoiled corn as a food appeared from the fact that in a few days there was a general loss in weight, which varied from 2 up to 7 and even 10 kilograms, though some showed an increase of 3 to 4 kilograms. In one case this increase may have been due to the cure of an old psoriasis; in another to great hunger, which caused the individual to eat more heartily.

Nervous and cutaneous symptoms showed themselves in some cases after the fifth dose, in others at the end of a week, and in some only at the end of two months. Two individuals were entirely resistive. On the other hand, one robust man showed acute poisoning with mydriasis, syncope and profuse diarrhea. In another an acute catarrhal condition of the stomach was developed.

Isolated disorders lasted for two and a half months after the suspension of the tincture. In one case they persisted ten months, but yielded finally to arsenic.

As a happy chance had shown the favorable action of this tincture on an old psoriasis, experiments in dermatologic therapy were made on forty-five patients to whom the tincture, and also the oil which is extracted from it, were administered internally

and externally. In almost all of these cases there appeared more or less difficult digestion, nervous phenomena and disorders of the cutaneous sensibility. Improvement in the cutaneous affections was *pari passu* with the appearance of toxic symptoms. This, then, would be an example of substitutive medication which sometimes cures or relieves certain chronic diseases by increasing the vaso-motor tone of diseased organs, and in consequence regulating trophic influences.

The principal gastro-intestinal, nervous, and cutaneous symptoms resembled those of visceral, spinal and ganglionic disease, while there were other symptoms evidently cerebral in their nature.

But the most important result of these experiments is the analogy between the symptoms observed and the clinical syndrome of pellagra.

#### ALCOHOLIC EXTRACT OR PELLAGROSINE.

To these first experiments must be added others made during the course of several years with the alcoholic extracts and the oil of spoiled corn, both derived from the tincture. These new investigations of Lombroso, in collaboration with Duprè, made with the glutinous and resinous substances gave no results in either man or animals. The toxic substance, or pellagrosine, however, given to dogs and chickens in doses of 5, 10 and 15 centigrams produced droopiness and diarrhea; in man, torpor, anorexia and nausea, accompanied by diarrhea.

With very careful preparation one can obtain with pellagrosine constantly a toxic action on animals.

**EXPERIMENTS ON FROGS:**

In frogs clonic convulsions appeared half an hour after the injection of pellagrosine in a strong dose of 50 centigrams. At the end of an hour there were increased motor reflexes and sensible diminution in the cardiac pulsations. Two hours later the movements of the heart gradually diminished and a tetanic state supervened which increased till death. In other experiments it was noted that at the end of a quarter hour the frog took a vertical position in the water. If placed on its back it did not turn over and displayed fibrillary contractions of the lower limbs; at the end of a half hour complete narcosis appeared; after three-quarters of an hour anesthesia to the strongest stimuli; one hour later tonic convulsions, very much increased reflex excitability and a pronounced tetanic state; three hours later death. A very small frog after an injection of 5 centigrams died immediately.

In a great number of experiments there were found very notable differences in results, such differences being dependent upon the size of the dose and the time when the substance used had been prepared, whether in August or in September.

With small doses a tetanic state appeared in 90% of the cases, especially if the frogs had been placed in lukewarm water. Sometimes this state was preceded by paresis or perhaps death followed it in half an hour to 25 hours.

In the case of other frogs with doses of 25 to 100 centigrams tonic cramps appeared in all the cases and paresis of the extremities was produced to such an extent that the animals rested vertically in the water. In 27 out of 100 frogs tetanic convulsions, with narcosis, preceded death, which occurred usually in thirty minutes. In the cold months the substances had scarcely a visible effect and even that frequently was evident only on close examination. The influence of the temperature appears distinctly when the animals are kept under artificial conditions in cold or warm water.

In water at 3 degrees C. a dose of 5 centigrams caused only hesitation in movement and increased motor reflexes

at the end of six to twenty-four hours. The same result is produced sooner in water at 8 degrees C.; at 32 or 36 degrees tetanic convulsions with death resulted from even small doses; and also from the blood of animals poisoned by pel-lagrosine, those injected remained stiff in water at 3 degrees and could not leap; at 32 to 36 degrees they were very lively at first, but soon became somnolent, though they did not die and did not show any tetanic condition; they succumbed, on the contrary, very quickly with tetanic symptoms, when placed in water at 38 to 42 degrees C.

For animals kept in lukewarm water the minimum lethal dose was 1 centigram per 14 grams of animal weight. The maximum dose without death was 50 centigrams per 12 grams of animal weight.

#### EXPERIMENTS ON BIRDS:

In general chickens showed a diminished sensibility to the effects of the substances.

In the case of a pigeon death occurred after a dose of 4 grams per kilogram, with clonic convulsions, preceded by narcosis, somnolence and diminution of temperature. The blood of this pigeon, still warm, injected into a frog, produced tetanic symptoms. In the case of hawks death occurred after a dose of 2 grams per kilogram, with diminution of weight, narcosis and tonic-clonic convulsions.

#### EXPERIMENTS ON RODENTS:

In case of rats doses of 12 grams per kilogram given internally remained without results; on the other hand, the same dose administered subcutaneously produced torpor, anorexia and paralysis of the hind legs with unilateral contractions; they fell on the right side and when they tried to move they rolled or sometimes walked backwards. Later complete paralysis and notable diminution of temperature. Convulsions appeared in only two rats after the absorption of 2.8 grams per kilogram of the poison. In three others with somewhat larger doses, death occurred at the end of one to thirteen hours.

The autopsy showed hyperemia of the spinal cord, pia mater, liver and kidneys, once also of the lungs; in one case softening of the cord was found. In the case of guinea pigs the minimum lethal dose was 2 grams per kilogram, but death did not occur until twelve hours later. In the case of three out of six of these animals tetanic convulsions appeared, preceded or followed by paralysis. Heat seemed to favor narcotic, as cold did tetanic phenomena.

#### EXPERIMENTS UPON CATS:

An experiment made upon one adult cat only with a subcutaneous dose of 1.4 grams per kilogram of the most active preparation caused death in ten hours. Soon after the injection immobility set in with refusal of food and rigidity of the hind legs. It was only at the end of three hours that there appeared tremor, then tetanic convulsions, hyperesthesia, increase of temperature (2 degrees) and, two hours later, coma. At the autopsy—hyperemia of the brain, spinal cord, liver and kidneys.

#### EXPERIMENTS ON DOGS:

In cases of dogs the results were also convincing. With doses of 2 grams per kilogram repeated vomiting occurred after a half hour to two hours, also contraction of the hind legs, dilated but mobile pupils, increase of sensibility and of motor reflexes—two hours later general tetanic convulsions, acceleration of the pulse and respiration and lowering of temperature. After each attack of tetanic convulsions the dog loses his equilibrium, crouches on the hind quarters and presses his head and paws against the ground. Experiments with other dogs gave similar results.

At the autopsy there was found hyperemia of the meninges, optic thalamus and of the gray matter of the spinal cord; in one case softening of the lumbar cord; twice ecchymoses of the lungs and congestion of the liver; once only hyperemia of the entire brain.

The following table is a résumé of the experiments showing lethal doses :

In case of	Minimum of grams to the kilogram of body weight	Average	Average time of death in hours
Frogs. . . . .	1.5	2.4	6
Cats. . . . .	7.0	10.0	14
Pigeons. . . .	....	4.0	5
Hawks. . . . .	....	2.0	3
Rats. . . . .	2.3	13.0	5.4
Rabbits. . . .	....	2.3	2.3
Guinea Pigs..	....	2.3	1.2
Dogs. . . . .	1.82	2.0	11

#### OIL EXTRACTED FROM SPOILED CORN.

It is necessary to distinguish three different preparations made from the oleo-resin of spoiled corn: that of July and August which is very bitter, muddy, chocolate colored, with a strong smell, obtained from corn carried to the state of putrid fermentation; the oil of September, less colored, less bitter and having a normal odor, is extracted from corn less spoiled; finally, the oil extracted from yellow bread, which is solid at 19 degrees C., and the oil extracted from the embryos of the grain.

#### EXPERIMENTS ON FROGS :

It was found in more than a hundred cases that in experiments made during summer with the active preparations tetanic convulsions appeared at the end of four to ten hours in 50 per cent. of them. The dose of the preparation was .75 gram up to 1 gram with animals which weighed between 18 and 35 grams. To tetanic convulsions succeeded paralysis

of the hind legs in 5 per cent., narcosis in 10 per cent.; in 30 per cent. tetanic convulsions did not occur, but difficulty in leaping and exaggeration of the reflexes of the hind legs at first and later of the fore legs occurred. In 20 per cent. only narcosis occurred without spasmodic symptoms, but death always followed.

The same preparation, in dose of 1 gram for 23 grams of weight, injected into frogs kept in a room at 8 degrees C. in December, produced only mild and retarded symptoms. Tetanic phenomena showed themselves at the end of eighteen hours, and at the end of thirty hours death occurred. Other experiments in cold or warm water demonstrated that the symptoms of poisoning were much mitigated by cold.

If, before the injection, the heart was laid bare, there was found, as in the use of the alcoholic extract, that at the end of a half hour a retardation of the pulse occurred most marked on the appearance of tetanic phenomena.

The same tetanic phenomena appeared after injection was made in a rat whose brain had been removed; partial section of the cord prevented spasmodic phenomena on the corresponding side. The members remaining in nervous connection with the rest of the body, but not with the circulation, exhibited constantly tetanic symptoms.

The urine and blood of animals having had injections of the alcoholic extract as well as the oil, produced tetanic phenomena in frogs, though the animals themselves remained free from toxic symptoms.

#### EXPERIMENTS ON CHICKENS:

These experiments are important because of their duration. In one chicken with a subcutaneous injection of the oil there were no motor symptoms; but it was droopy all day and had diarrhea. A cock behaved in the same manner. When given by the mouth, this substance had a less marked effect; however, it arrested increase in weight in young fowls. In one untreated chicken the weight increased 200 grams from the 20th of November to the 2nd of December, but under treatment with the oil from the 3rd to the 16th of December the increase of weight was only 100 grams.

Finally, after five months of interrupted administration of the oil, there appeared choreiform movements of the head, previously observed in the experiments with Dupre. In the case of one chicken choreiform movements of the head appeared at the end of ten days; with repeated doses the motor derangement became general—it walked backwards, raised the feet slowly and in an exaggerated manner, and had a tendency to walk very near the wall. Then eczema of the comb appeared with diarrhea, increase of temperature after the injection, defervescence in the intervals; the chicken died with typhoid and paralytic phenomena. At the autopsy were found intestinal hemorrhages similar to those seen in septic poisoning.

#### EXPERIMENTS ON MAMMALS:

With four rats one dose of 5 grams brought about subnormal temperature with paresis, contractures, and once death following paralysis of the hind legs. A cat, after a dose of 4.9 grams per kilogram, had photophobia and refused food. With larger doses (6 gr.) loss of appetite, paresis, decided photophobia and death at the end of two days, with loss of 40 per cent. in weight.

In the case of a bitch, after an injection of 20 grams, tonic convulsions of the legs and paresis occurred in two hours. Three hours afterwards there remained only a decided reflex excitability, mydriasis, agitation, refusal of food and staggering gait. The next day there remained only difficulty in leaping, and walking with rigidity of the fore legs. In another dog, after an injection of 30 grams, torpor, rigidity of the hind legs and slight desire for food. In general, the oil produced the same symptoms as the alcoholic extract, although less in degree.

#### OIL EXTRACTED FROM MOULDED BREAD.

The oil of moulded bread produced the same symptoms as the maximum grade of oil of corn prepared in August. In a single experiment it was more active.



### EXTRACT OF THE EMBRYOS OF SPOILED CORN.

This oil, or rather fat, produced symptoms similar to those produced by oil made from the entire grain, but larger doses were required.

### OXIDIZED OIL OF CORN.

The rancid oil of corn has produced various results, physiological and toxic; these results have been confirmed by the investigations of Biffi; they are: diminution of weight and increase of temperature. In frogs temporary torpor was produced with an injection of 2 grams. The effects are variable according to the quality of the corn used in making the oil. Control experiments have been made by injections of olive oil and oil from fresh and sound corn. The results were negative.

### AQUEOUS EXTRACT OF SPOILED CORN.

The aqueous extract has an antifermentative action analogous to that of the alcoholic extract, though more feeble. The effects on the animal organism are also less intense.

In frogs, after large doses (70 to 75 centigrams) were injected, there appeared paralysis of the hind legs, generally temporary, fibrillary twitchings, narcosis and death at the end of three-quarters of an hour. A smaller dose (30 centigrams) produced the same symptoms, but required a longer time. At the end of three hours fibrillary twitchings set in, then paresis and at the end of six hours death.

Diminution of the cardiac pulsations is noted one-quarter hour after injections. Doses of 5 grams per kilogram to

cats produced vomiting, narcosis and loss of weight. After doses of 8 grams per kilogram death at the end of a half-hour, preceded by clonic and tonic convulsions.

At the autopsy was found hyperemia of the liver with fatty degeneration of the kidneys, once hyperemia of the base of the brain and ecchymoses of the lungs.

In the case of five dogs the symptoms were almost identical. By mouth no effect was noted till the dose of 8 grams per kilogram was reached, when narcosis and tremor appeared. Subcutaneous injections always produced abscesses; in doses of 5 grams per kilogram death occurred in fourteen hours.

In brief, the symptoms preceding death, especially the nervous symptoms, were, in four dogs out of five, identical with those produced by the alcoholic extract. In one of the dogs loss of intelligence was preceded by deafness; twice erection was produced. The five dogs held the hind legs apart, refused food, and had a reduction of temperature from two to eight degrees.

The autopsy showed twice extravasation at the base of the brain, hyperemia of the spinal cord, principally of the gray matter, and congestion of the stomach and liver.

### ALKALOID OF SPOILED CORN.

The alkaloid, analogous to strychnine, extracted from the oil by Erba, was injected in a dose of 2 milligrams into frogs; tetanic convulsions appeared in twenty to thirty minutes. On the other hand, the rate of cardiac pulsations did not diminish as much as in the experiments with other substances, perhaps owing to the more rapid action of the poison. The alkaloid taken directly from bread of spoiled corn killed a frog with tetanic symptoms in forty minutes in dose of .0025 grams. After the extraction of the alkaloid the residue is still poisonous in small doses—a thing which proves that

the isolated alkaloid is not the only poisonous substance of corn.

#### EXTRACTS OF ORDINARY CORN.

Pellizzi has made a number of experiments, bacteriologic, chemical and toxicologic, which confirm the preceding. [A number of workers have confirmed Lombroso's experimental work in a general way, such as Erba, Hausemann, Pellogio, Gosio and Ferrati, Mariani, Belmondo, Tirelli and Babes and Sion.] He isolated numerous micro-organisms from corn meal more or less spoiled, and he concluded that the development of numerous colonies of diverse bacteria can be prevented only by drying the corn in ovens heated to 70 degrees C. for several days before being ground. Some meals, having all the appearance of originating from good corn and showing a bright surface like that which has been dried a long time, contained often more bacteria than other meals which had appeared to be spoiled. The apparently sound meals were, therefore, notwithstanding appearances, just as spoiled and dangerous as those more clearly damaged. Pellizzi prepared toxines of sterilized cultures of these micro-organisms for subcutaneous and intravenous injections into rabbits and dogs. Sometimes he employed pure bouillon cultures, at other times mixed. Certain cultures, such as those of diverse hyphomycetes, the *saccharomyces sphaericus albus* and of the *bacillus subtilis*, did not cause particular derangements; the *bacterium maidis* produced results similar to those obtained by others who had worked with it; preparations made,

however, from cultures of micro-organisms allied to the putrefactive bacteria produced, chiefly in dogs, phenomena analogous to pellagrous poisoning in man.

The results of this work seem to show that the important bacteria of spoiled corn resemble the putrefactive bacteria and that bouillon cultures of them contain only organic nitrogenous substances in decomposition. The results could then be attributed exclusively to putrid substances and not to a specific poison of spoiled corn.

Pellizzi, therefore, did not continue his researches with these cultures, but with the aqueous extracts made from polenta and from corn bread prepared from meal bought in the stores which furnish the tables of the people. Examined bacteriologically this meal contained numerous putrefactive bacteria such as are found in spoiled corn. As a control experiment aqueous extracts of wheat and of rye bread were used, but without results.

Extracts of polenta and of corn bread were placed for eight hours in a damp chamber; examination revealed the presence of numerous forms of micro-organisms of corn.

The effect of these preparations was tried on dogs by the mouth, subcutaneously and intravenously. The most interesting results, which we shall abridge here for want of space, were from intravenous injections. If injections are made intravenously into an animal, in a dose of 10 grams per kilogram of weight, of aqueous extract of a polenta meal contaminated bacteriologically, but still edible, one pro-

duces, especially in dogs, grave pellagrous manifestations: paresis, gastro-intestinal disorders, psychic confusion. The same extracts made from materials previously placed for six hours in a Koch sterilizer become inoffensive.

It is evident from all of the experimental work that constant and characteristic effects have been obtained by the use of extracts of spoiled corn, or of its products.

The facts recognized by statistics and by clinical observation are not always easy to reconcile. The statistics show that only in the case of 25 per cent. of pellagrins can it be affirmed with certainty that they were nourished with food consisting principally of corn very badly spoiled. On the other hand, clinical observations demonstrate that it is not rare to see cases of severe pellagra in persons well nourished and in good circumstances, of whom it can be said that they do not habitually eat spoiled corn. Finally, there are recrudescences of pellagra with grave symptoms when the convalescents return to nourishment with corn, even when the corn consumed answers to the most severe hygienic demands.

These experiments prove the existence of micro-organisms either in a developed form or in the form of spores in the grain and meal of corn which have the very best appearances and are habitually used for human food. It can then be supposed that the elements necessary to the production of the pellagrous symptoms, once having entered into the circulation, are there decomposed under the action of ferments found in the organism, and undergo, after



Plate VII. South Carolina case. "Wet" dermatitis. Localization unusual. Hands edematous. Cachectic stage.



absorption, toxic transformations. It cannot be determined, according to Pellizzi, what is the nature, in a given medium, of the products of the bacteria found on corn. Do they constitute a chemical poison in the strict sense of the word; or, as is more probable, do they belong to the amorphous chemical ferments, which can be produced at a determined phase of their development? For many similar ferments complex actions have been found; Pellizzi found them in his extracts of corn. It is reasonable that the harmful effect does not come from a pure culture of one organism, but from a mixed culture of several varieties. It is a question, certainly, of a combined and probably mutual action, not yet defined. If a toxic substance could be directly drawn from edible corn without mixture with putrid substances in the strict sense of the word—then the features of pellagrous poisoning can represent a polytoxic state. Finally, it is necessary to take into consideration the most complex and various facts and to give to spoiled corn a very wide definition. Almost all corn, with very few exceptions, can thus be considered spoiled corn to some degree. Corn, absolutely sterilized, if one could have it, would certainly be harmless, and of course the meal also. But if it is difficult to have corn entirely dry, it is certainly impossible to keep it in this state, for as soon as the places in which it is stored reach a certain degree of humidity, the most diverse micro-organisms find favorable conditions for their development.



In concluding his experimental work Lombroso states that "with such evidence as has been submitted it does not seem longer possible that the specific cause of pellagra can be doubted, and it is certain that the etiology of other maladies can present documents neither more numerous nor more convincing."

[The author has necessarily given to a large extent only Professor Lombroso's ideas on the etiology of pellagra, and Lombroso's labors in this field entitle his ideas and opinions to the highest admiration and respect. He has, he tells us, spent more than twenty-five years of his life at it, and that these years have not been fruitless is abundantly witnessed wherever the disease has perplexed and taxed the medical man and the sanitarian. His scientific work is of a high order and his hypothesis as to the etiology of pellagra has had a profound effect not only in purely scientific fields but also has resulted in great organized endeavors to limit and eradicate a disease which has been a burden on Italy for a long period of years.

Notwithstanding this, there are other important ideas on the etiology of pellagra which should receive some consideration. The subject is by no means a closed one. And it would seem wise that the American reader, to whom the subject is to some extent new and unfamiliar, should get a general view of the etiological field.

A recent Italian writer has said: "The actual knowledge of the cause and nature of pellagra, one may say, remains still in the realm of hypothesis, although an extraordinary scientific activity on the

part of students, especially Italian students, has thrown light on many important points." That is to say that in any definite scientific sense the etiology of pellagra is still essentially unknown. This, however, is very far from saying that nothing is known of its etiology. There is, on the contrary, a profound and general conviction, among students and authorities, that between pellagra and the use of Indian corn as food there exists some definite, etiological relation, the ultimate nature of which, however, still remains in doubt. With the exception of a small group of students, to whom reference is made later, practically all theories of etiology take into essential consideration the use of corn or its products as a food.

This idea of a causal relation between corn and pellagra is almost as old as the history of the disease itself, and such a suspicion is thought possibly to have been entertained even by Casàl himself, as has been noted previously. Indeed, there are authors who are inclined to maintain that the disease was known before Casàl's day and that even then similar suspicions were entertained. It was perhaps first formulated by Marzari (1810), who believed that corn caused the disease by reason of its deficiency in certain nutritive qualities. And with this early declaration very soon came into existence the great corn theory of pellagra, and the ultimate creation of the so-called "Zeist" (from *Zea Mays*) and "Anti-zeist" schools of thought. Between these opposing schools a wordy war was waged for many years and echoes of it still linger, but from that time

till now the corn idea, in one form or another, has held the dominant place in the etiology of pellagra.

Following its definite enunciation, the corn doctrine, more or less rapidly, began to undergo a development and modification which has continued up to the present time with a consequent almost bewildering variety of opinions.

The first and one of the most important steps in its evolution was the announcement of Balardini's "Verderame" theory. Balardini had noticed on the grain a greenish discoloration (hence "Verderame") which was found later to be due to the growth of a mould, *Sporosorum maidis*; and he conceived the disease to be due to this mould. This introduced an entirely new phase of the corn theory in attributing the disease not to corn *per se*, but to spoiled or damaged corn. Later, Lombroso, doubtless under the stimulation of Balardini's work, took up this idea and developed it broadly, creating ultimately what is sometimes called the "Zeitoxic" school, who maintain that not in corn, but in *spoiled* corn, must the cause of pellagra be sought.

Without attempting to trace historically the evolution of the corn doctrine, it will perhaps serve every purpose to state, somewhat briefly perhaps, the important etiological views held on the subject by students of the disease. In the preceding pages Marie has given somewhat at length the general character of the evidence on which is based the broad idea of an etiological relation between corn and pellagra, so that need not detain us longer.

Now, disregarding some of the fine and unimportant distinctions, we may place the various modifications of the corn theory into a few general groups, some of which may be dismissed with very few words.

1. The idea that corn, as a food stuff, is wanting in proper nutritive value. This conception, at one time of rather wide importance, had finally to be abandoned when it was shown by careful analysis that this cereal possesses high nutritive value, is rich in fats and nitrogenous substances and easily assimilable (further reference is made to this in Chapter IX). It is also to be noted that not infrequently pellagra is found among well-nourished individuals and its early symptoms are not those of inanition.

2. The idea that good sound maize contains certain toxic substances which cause pellagra. This idea also was discredited by the absence of pellagra in many places where corn for long periods of time had been extensively used as food.

It is worth while to note here, however, the important fact that the gross distinction between sound and spoiled corn is, in the opinion of many able observers, by no means always easily determined. The grain by reason of its rather poorly protected embryo and its high fat and nitrogen content readily undergoes change under the influence of bacterial growth. Pellizzi and Tirelli, after an extensive experimental research, divided spoiled corn into three classes: (a) corn evidently and profoundly altered; (b) corn apparently little altered; (c) corn apparently normal. These changes in corn take place all

the more readily, of course, in the presence of moisture; hence the importance of properly curing and storing the grain.

3. The toxicochemical idea that corn by reason of parasitic growths (bacteria or moulds) may undergo change with the formation of one or more toxic substances of a chemical nature (exogenous poisons). In other words, instead of an infection of the body with the elaboration of toxins within the organism, we have, so to speak, an infection of the corn with elaboration of toxins outside of the body, which are toxins nevertheless and when introduced into the organism produce their characteristic effects, though the bacteria which produce them may be in themselves harmless to man.

This is the great and important Lombrosian idea and has been fully discussed in other places. It has had a profound effect on the problem of pellagra, and has attracted a host of adherents.

It is only fair to say here, however, that the experimental work of Lombroso and others has not escaped criticism at the hands of many earnest and capable men. There are not a few who think that such experimental evidence is inconclusive, and that the disease picture reproduced in animals, and even in man, while it may be similar to pellagra, is not necessarily the disease itself; and that such poisons are not as yet clearly shown to be specific. For example, Gosio, in reviewing the subject of etiology recently, said: "Indubitably the various toxic moulds of corn have the power of producing a form of poisoning, which has many points of contact with

pellagra; but if this be in reality pellagra or such pellagra as is observed in practice, if the syndrome which happens to be reproduced in animals by poisons of moulds represents without doubt the specific pellagra of man, it yet remains rigidly to be demonstrated." And again he says: "Always, however, one speaks of a proof which does not make a break in the true nucleus of the problem, which is the demonstration of the chemical identity between poisons circulating in the blood of a pellagrin and the poisons of moulds."

It is of great interest in this connection to know that Babes and Manicatide, as well as Antonini and Mariani, have, from a series of careful experiments, concluded that there exists in the blood of cured pellagrins a specific antitoxic power against the poisons of spoiled corn.

4. The toxicoinfective idea that from spoiled corn there is formed within the body certain toxic substances (endogenous toxines). With this view the disease becomes in reality a form of auto-intoxication, or perhaps an intestinal mycosis.

Neusser, for example, in certain cases advocated the idea that there is formed in corn, largely by the *Bacterium maidis*, a certain "receptive mother substance" which later in the gastro-intestinal tract underwent a further change and so became toxic; and De Giaksa, as well as Di Donna, have laid stress on the importance of the colon bacillus, supporting the idea that the vegetating properties of this bacillus may become greatly modified on a culture medium of corn, with the consequent production in

the intestinal tract of specific substances. Marie, as we have seen, also seems to favor to a certain extent a possible idea of autointoxication.

5. The idea that pellagra is a specific infection, either by moulds or by bacteria, derived from corn, or usually derived from that cereal.

The flora of corn, as we have seen, has received a great deal of attention, and it is needless again to refer at length to that here. There remains, however, the more or less recent work of two men which seems of sufficient importance to justify notice. These are Ceni and Tizzoni.

In 1902 Ceni declared pellagra to be due to an infection by two moulds, *Aspergillus fumigatus* and *flavescens*—a true aspergillosis; or a “toxico-parasitic” disease.

Ceni has written quite extensively on the subject and his work has attracted a great deal of attention. His conclusions are based on elaborate and carefully conducted experiments on animals, the details of which can not be given here.

It has seemed to many that with his ideas at last some adequate explanation of the real nature of the malady may ultimately be achieved. The essential parts of this hypothesis will serve to show the reader its scope. It is a significant fact, however, that his work has not yet been confirmed.

Ceni states that individuals who die with the characteristic phenomena of pellagra, either in the acute or subacute forms, succumb almost always as a consequence of an aspergillary infection; and that this infection, localized generally in the lungs,

pleuræ, pericardium, pia mater, or mesenteric glands contributes the determining cause of the morbid phenomena exhibited by the sufferer.

The pathogenic agents of this infection are represented especially by the *Aspergillus fumigatus* and the *Aspergillus flavescens*, which usually act each by itself and rarely together in one infection.

These parasites, ingested with food, pass through the intestinal wall in the state of a spore, and, as such, localize in the various organs or tissues. Locally they set up a true inflammatory process, and they elaborate very virulent poisons which give rise to the general intoxication.

The gravity of these morbid phenomena is in direct ratio with the pathogenic power of the two species and the state of their virulence, which latter seems to depend on the season of the year. The *Aspergillus fumigatus* appears to be the more pathogenic of the two, and its state of virulence is greatly heightened in the spring months, while the *Aspergillus flavescens* displays its greatest poisonous properties in the fall. In both cases this season corresponds to the "cycle of the annual biologic evolution" of the two moulds, and it will be noted that this heightened virulence corresponds also to the seasons when pellagra shows its most severe and characteristic symptoms in man.

Regarding the relation of these pathogenic moulds to corn, Ceni states that food prepared from corn which is infected by these parasites, constitutes a direct cause (*concausa*) along with the moulds, the corn thus serving as a means of infecting man by



way of the intestinal tract. And further that food infection by these micro-organisms is in direct ratio to the unhygienic surroundings in which such food is prepared or stored. His idea seems to be that while corn may not be absolutely necessary as a means of conveying this infection it is nevertheless in all probability a very important and general method of doing so, at least in Italy. And furthermore that corn is a particularly favorable medium and the parasites which develop on it and are eaten with it seem to possess a virulence much more exalted than others which grow on other substances.

Not only in these moulds but in other varieties of *Aspergilli* and *Penicillia* virulent and characteristic toxins have been found and such moulds are regarded as pathogenic, but the *Aspergillus fumigatus* and *flavescens* alone seem to possess the power of invading and infecting the body. All other varieties appear to elaborate their toxins in the intestinal tract and so poison the organism from this place.

Ceni has also declared that in all pathogenic moulds the season of the year plays the same important part as in *Aspergillus fumigatus* and *flavescens*; and the micro-organisms are most virulent at the culminating phase of their development. Moreover, the various moulds or their varieties produce often toxins quite different in character. For example, there seem to be two varieties of *Penicillium glaucum*, one variety A, and another B. The A variety produces characteristic depressive phenomena (general depression, muscular relaxation

with diminution of tone, etc.), while the B variety, on the other hand, gives rise to exciting symptoms (exaggeration of reflexes, general tremor, spasmodic state of musculature, etc.).

Finally, these moulds seem able to withstand quite high temperatures, a fact of importance in connection with the usual cooking of corn before its consumption.

It may be added that Ceni's statements with regard to seasonal virulence of moulds hold good for the Italian climate in which he did his work. Climatic conditions in this respect seem to exercise much influence and should be taken into consideration.

Tizzoni also considers pellagra an infection, but a bacterial and not a mould infection—the specific micro-organism is called the *Strepto-bacillus pellagrae*.

It is a small, short bacillus generally, but seems to be somewhat irregular in its form, grows in long or short chains or groups, colors well with the usual aniline dyes, often showing polar staining. It does not form spores, and grows best at 37 degrees C. on human or rabbit blood agar, but is said to resist a temperature of 80 degrees or even 90 degrees for one hour.

There seem to be two different, distinct strains or types of the micro-organism, readily distinguished by cultural methods. One of them corresponds to the acute phenomena of pellagra and the other to the more chronic states. The bacillus is pathogenic for the usual laboratory animals, but is most character-

istic in the guinea pig; and its toxins show a long period of latency.

This organism was first isolated from the blood and organs of acute pellagrins, but later (1909) also from the stools and blood of chronic pellagrins, as well as from spoiled corn.

In feeding experiments on animals the morbid picture of pellagra was reproduced distinctly in the guinea pig, but only when a liberal share of corn was added to the food of the animal.

The infection then is derived from spoiled corn. The elective lesion is in the intestine which is always primarily involved. This intestinal lesion is always followed by a specific, general intoxication which is especially manifested upon the nervous system, the blood vessels and the red blood cells; and secondarily upon the liver and kidneys. The toxins are said to have a particular affinity for the nervous system, conducing ultimately to its profound disintegration.

This micro-organism may, as Marie has suggested, be only a secondary invader. Tizzoni's completed work is too recent to have received much critical notice as yet.

In our work we have been unable to isolate this micro-organism after repeated trials. In fact, all cultural methods with both blood and spinal fluid have with us been negative, nor have we had better success with animals.

So much for the maize theory and its variations. Now when we turn to the "antizeists" we find them greatly in the minority. There are two great facts

which have been urged against the corn theory. First, and most significant, is the extensive territory over which corn is, and has been cultivated and used as food for many generations, and yet no pellagra has appeared. The second is the frequently reported cases of pellagra in which there is no history of the use of corn or its products as food by the sufferers from pellagra.

The first statement is of course evident, and the "zeitoxic" idea is offered in explanation. The second is by no means always admitted, and has proved the cause of much controversy. Soon after its creation the "zeist" idea met with much opposition, and later a group of French thinkers, led by Landouzy and others, reported a number of cases of pellagra where no corn had been consumed. Roussel, the able and ardent French "zeist," sharply questioned such observations and rather effectually discredited the diagnosis, introducing at the same time into the literature of pellagra the now well known term pseudopellagra, which he thought described their cases, as they did not conform to the picture of the true disease. This term, pseudopellagra, has itself been the cause of confusion to some and an object of ridicule to others. Manson speaks of the invention of the comfortable term pseudopellagra, and scornfully remarks: "The disease is pellagra when it fits in with the orthodox theory and when it can be connected in any way with maize, but when this is not possible, the disease becomes pseudopellagra."

From France frequent reports have been and are being made of pellagra without corn, and there has grown up there a school of thought which denies that pellagra is a morbid entity at all. It is spoken of as the pellagrous syndrome and regarded as a *morbus miseriae*. It is undoubtedly true that there may arise among alcoholics and in cachectic states, especially among the insane, certain symptoms simulating in many respects pellagra, yet such a diagnosis is not admissible; and it is said that a careful study of such cases readily permits discrimination. Certainly it seems difficult to understand how doubt can arise that pellagra is a disease *sui generis*, when consideration is given to its unique symptomatology, its anatomical lesions, epidemiology, and geographical distribution.

All criticism of the maize school, however, is not of this destructive type. At the meeting of the British Medical Association in 1905, Sambon, in a notable paper, put forward the highly interesting suggestion that pellagra might be due to some protozoon, a suggestion which has later met with the hearty approval of Manson. The general line of this argument is that an examination of the numerous observations and experiments shows one fact clearly, and that is that each investigator asserts that he has produced pellagra, either in man or animals, and yet it is evident that the disease can have but one cause. It is unwise, therefore, to place too much reliance on such experiments, and it should not be forgotten, as history amply shows, that the interpretation of experiments is often as fallacious

as the interpretation of natural facts. The reputed historical facts with regard to the relation between the introduction of corn culture and the appearance of pellagra are called in question, and an attempt is made to show that there is historical evidence to prove that corn was grown in Europe long before the date usually assigned. It is pointed out that the areas of corn growing and pellagra endemicity do not coincide, that pellagra has been observed frequently in parts of France, Spain, and Italy where corn is not cultivated, and that the comparative study of the distribution and prevalence of pellagra at different periods is decidedly unfavorable to the corn theory.

The opinion is expressed that the prevailing ideas as to the etiology of pellagra are very unsatisfactory, and that the corn idea has been much too dogmatically adhered to by investigators. The suggestion is made that pellagra shows many analogies with such diseases as syphilis, trypanosomiasis, and kala azar. Such remarkable resemblances are noted between pellagra and trypanosomiasis as the characteristic, perivascular, small cell infiltration, benefit by treatment with arsenical preparations, and the mononuclear increase in the blood. It is further suggested that the parasite may be insect borne, and the erythema of pellagra may be one of those interesting instances of correlation in nature whereby the parasite is enabled to enter some intermediate host, complete its life cycle, and perpetuate its existence, such as is seen in the correlation between the night swarming of the larvæ of certain filaria and

the nocturnal habits of its intermediate host, the mosquito; and that corn may perhaps be found to sustain some such relation to the etiology of pellagra as the swamp has been shown to sustain to the etiology of malaria.

In this connection it is highly interesting to record that Babes and others in a very recent article have reported highly beneficial effects in the treatment of pellagra by atoxyl and arsenous acid combined, and they have put forward practically the same suggestive idea as Sambon's. They state that the almost specific therapeutic action of arsenical preparations as well on certain protozoal diseases as upon the manifestations of pellagra at least suggests, by analogy, some conclusions as to a similar etiology. Pellagra, they still think, is in all likelihood due to some change in corn caused by parasitic influence, and the idea can not yet be excluded that from spoiled corn not only toxic substances but parasites as well may be conveyed to the pre-disposed human organism, either direct or by means of insects or other organisms.

From its analogy to malaria, piroplasmosis, and trypanosomiasis, diseases to a certain extent with the same geographical distribution, the thought is justified that for the transmission of pellagra some similar, intermediate, animal host is necessary; and for the intoxication or infection itself some microscopic animal parasite. Such a parasite must necessarily be very small, perhaps ultramicroscopic, and, although in their researches they found only in the erythematous skin of pellagrins bodies resembling



Plate VIII. South Carolina case. Skin of hands dry and thickened. Marked seborrhea of nose and face. Extreme emaciation of cachectic stage. Death followed in a few days.





the smallest Negri bodies, yet the results of arsenical treatment encourage new investigations along the lines suggested.

In a very recent note on *diplodia* disease of corn by Smith and Hedges of the Agricultural Department, the suggestion is made that this fungus may have some connection with pellagra. The *diplodia* seems to be a fungus which infects the soil and enters the grain from the interior of the plant, that is, by way of the root system, stem and cob. The fungus persists from year to year in infected fields and certain soil conditions seem to favor or prevent its entering the plant. This mould seems quite extensively found on corn in the United States. Tiraboschi, as noted, has found it only on imported corn in Italy.

Von Deckenbach, as stated by Professor Lombroso in his preface to this volume, has recently found *Oospora verticilloides* widely prevalent on corn in Bessarabia. From experimental work and investigation he regards this mould of great etiological importance and seems even to think that it will be found to bear the same relation to pellagra as does the *claviceps purpurea* to ergotism.

To sum up, then, it may be said that while the real nature and cause of pellagra still remains in doubt, there is, nevertheless, a firm and almost universal belief that the disease is in some way connected with the use of corn as an article of food—a belief so universal as to render its rejection well-nigh impossible except in the face of demonstrative proof to the contrary. Ceni's work and ideas, in the present

state of our knowledge, have attracted great attention, and in their light many obscure points seem to have received illumination, but they still await confirmation. Tizzoni's specific bacillus must yet stand the test of time. Sambon's idea rests only on an argument by analogy and is at present little more than a suggestion, but a highly interesting one. It may possibly lead to important developments at the hands of investigators.

Before closing the subject, however, it seems proper to introduce here some of the details of Sambon's more recent investigations.\*

While of course the great majority of the Italian medical world hold the view that there is some important, if not well understood, etiological relation between pellagra and the use of spoiled corn as an article of diet, there are nevertheless at least some students of the disease who have begun seriously to question such an etiological relation. And this has resulted in a perceptible tendency, more or less strong among certain students of pellagra, to disregard corn entirely as an etiological factor in this disease and to seek some new idea to explain its occurrence. This tendency is in the direction of some protozoal or animal parasite and has been, in all likelihood, produced and stimulated by the ideas of Sambon, first expressed in 1905.

Recently there has been formed a British commission for the study of pellagra, and Sambon was sent to Italy to try to establish his views on the etiology of the disease.

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\*This account is abstracted from Public Health Reports, XXV, 735, Wash., 1910.

Sambon's theory has been worked out much more in detail than when first presented, in 1905, and has attracted much serious attention. His work in Italy, largely of an epidemiological nature, has greatly strengthened him in his belief in the accuracy of his theory and he feels confident of its ultimate proof.

Succinctly expressed, this theory in its main features is as follows, the details having been kindly furnished by Doctor Sambon:

Pellagra is not due to maize, either good or bad, because—

1. It is found in places where maize is neither cultivated nor eaten.

2. It is absent from many places where maize is the staple food of the population.

3. It has in many places either decreased or become more prevalent without any change in the food of the people.

4. Its constant and peculiar distribution does not agree with the very irregular and ever-changing distribution of spoiled maize.

5. In over a century and a half, since the maize theory was first suggested, no one has been able to prove it.

The belief that the disease has everywhere followed the introduction of corn cultivation is unfounded. Pellagra was first recognized as a specific disease in the beginning of the eighteenth century, but this does not prove that it was not prevalent long before that time.

Pellagra is a parasitic disease because:

1. For years the person affected may present some

seasonal recurrences, which can only be explained by a parasitic agent with alternating periods of activity and latency.

2. It shows a constant and characteristic topographic distribution.

3. It shows a definite seasonal incidence.

4. Its symptoms, course, duration, morbid anatomy, as well as its therapy, are similar to those of parasitic diseases.

5. Of two places, almost contiguous, one may be affected, the other not.

Pellagra is an insect-borne disease because:

1. It is limited, like malaria, sleeping sickness, etc., to rural places and more especially to the vicinity of certain bodies of water.

2. It has a definite seasonal incidence—spring and autumn.

3. It affects, to a large extent, a certain class of people—the field laborers.

4. It is not contagious and neither food nor water can account for its peculiar epidemiology.

5. Within its endemic centers it affects all ages and frequently whole families.

6. Outside its endemic centers only adults who have visited the infection areas present the disease and frequently only one or two members in a family are affected.

Pellagra is conveyed by *Simulium reptans* because:

1. *Simulium* is found in the torrents and swift running streams of all pellagra districts.

2. *Simulium* has the peculiar seasonal distribution of pellagra (spring and autumn).

3. *Simulium* is found only in rural districts. It is unknown in towns and villages. It does not enter houses.

4. *Simulium* explains most admirably the peculiar limitation of the disease to field laborers.

5. *Simulium* is the only blood-sucking insect which the British field commission has found in its visits to numerous pellagrous districts in Italy.

6. *Simulium reptans*, like *Anopheles maculipennis*, has a world-wide distribution and explains the wide distribution of pellagra. It is found wherever pellagra is found.

7. *Simulium* causes epizootics in animals in America and in Europe.

8. Professor Mesnil has found a protozoal organism in *simulium*.

The judicial mental attitude which American investigators have so far shown with regard to the etiology of pellagra is certainly to be commended in the present unsatisfactory status of this question. The etiology of pellagra is still an open question. The belief that the disease bears some relation to spoiled corn has so dominated the etiological field and has received the support of so many men of wide experience that it can not be now entirely disregarded; but certainly it need not be accepted with so complete a dogmatism as to prevent investigation along other suggestive lines.

The theory of Sambon is of great interest, and it seems that now, when this theory has been elaborated so much more in detail, it is well worthy of serious attention at the hands of American students and investigators.

In a presumably semi-official account of Dr. Sambon's three months' work in Italy\* it is stated that he carried out his epidemiological survey in the provinces of Milan, Bergamo, Brescia, Padua, Rome and Perugia. As a result of his investigations Dr. Sambon entirely repudiates the maize theory. According to Dr. Sambon, pellagra is linked to the running stream just as malaria is linked to the swamp. He claims to have proved that the sand-fly (*Simulium*) explains the epidemiology of pellagra, just as the mosquito (*Anopheles*) explains that of malaria.

As bearing upon the geographical distribution of sand flies we have the opinion of so high an authority as Dr. L. O. Howard, chief of the bureau of entomology, U. S. Department of Agriculture, Washington:

"*Simulium reptans* does not occur in this country. Its only extra-European locality is Greenland, I believe. The genus *Simulium* is represented in this country by twenty-seven species. In my opinion Dr. Sambon is wrong in his conclusions."

Furthermore, we may quote from Dr. W. D. Hunter, of the same Department, now in charge of insect investigations in the Southern States: "All the information at hand at present seems to show that in this country there is no apparent connection between *Simulium* and pellagra. The centers where *Simulium* is most abundant are along the Mississippi Valley from Baton Rouge north to about Cairo and in New Hampshire, Maine and New York. From a

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\*Jour. Trop. Med. and Hyg., June 15, 1910, p. 180.

*priori* considerations, if there is anything in the Simulium theory, the centers of pellagrous infection in the United States should be in the localities mentioned rather than in the Southeastern States."

Naturally Sambon's theory may be expected to arouse controversy, especially among the Italians. Meanwhile, this announcement is interesting:

"Professor Alessandrini, of the University of Rome, who has been for years devoting himself to the study of pellagra, has just made a statement that he is now absolutely convinced that it is not corn which produces this terrible disease, nor is it in any way responsible for the malady, but that he has discovered the true parasites or germs of pellagra in water, which proves to his entire satisfaction that water is the vehicle of the disease and not corn, which has heretofore been regarded as the cause of the dread affliction."

In this connection it may be wise to quote from the Journal of the American Medical Association, LV 6, 543, this summary of one of the most recent contributions\* to the pathogenesis of pellagra:

"Raubitschek has been applying the biologic, anaphylactic, serologic, deviation of complement and other tests to determine the actual bases of the various theories in regard to the origin of pellagra. His extensive experimental work was done at the institute for pathology and bacteriology at Czernowitz. The constantly negative results show, he thinks, that none of the theories at present in vogue is correct. He then reports further research which

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\*Wien. Klin. Wochensh., XXIII, 26, 963.



seems to show that pellagra and beriberi are the result of the action of some toxine in corn and rice which does not display any toxic action unless it is sensitized by the chemical rays of the sunlight. Laboratory animals fed with corn or rice kept well so long as they were not exposed to direct sunlight, but under the influence of sunlight developed emaciation and paralytic phenomena, dying in from 8 to 21 days. He found that animals taken away from the sunlight, soon after the onset of symptoms, rapidly recovered, without change of diet. The anatomic and bacteriologic findings in the animals were constantly negative. He was led to this conception of the origin of pellagra as the action of an alimentary poison plus sunlight by the experiences with white animals fed on buckwheat. Kept in the dark they remained healthy, while when exposed to the sunlight the hair dropped out and the animals became emaciated and soon died with symptoms of paralysis. This syndrome was not observed with the dark-colored animals nor with those kept out of the sunshine. The similarity between this 'fagopyrism' and pellagra is more striking on account of the facts that the pellagra symptoms develop in summer with special intensity, that the skin manifestations are almost exclusively restricted to the parts exposed to the sunlight, that corn has more fat than any other grain, and that the active body in buckwheat is soluble in alcohol. He explains pellagra consequently as due to a toxine which develops in the parts of the skin exposed to the sunlight from the action of the chemical rays on the lipoid, alcohol-soluble element

in corn. The toxine developing in the skin causes the superficial lesions and has also injurious systemic action. He cites some analyses of wheat, rice and corn showing the proportions as follows:

	Dry			
	Water.	Substance.	Protein.	Fat.
Wheat. . . . .	13.6	86.4	12	1
Rice. . . . .	10	89.5	11.7	2.3
Corn. . . . .	10.2	90	15.2	3.8"

The discussion of etiology can not be concluded without some reference to predisposing causes. Predisposition in pellagra is admittedly a factor of much importance in the disease, yet it is often difficult to define with exactitude just what constitutes the strong predisposing points in individual cases.

Of course the immense importance of poverty and wretchedness, with all that is implied in these terms, is recognized by every one. Pellagra is, to a large extent, admittedly a disease of the poverty stricken. Simply to say, however, that a disease is associated usually with poverty is to be lacking somewhat in scientific definiteness. A great many different, if not diverse, factors are to be found under such conditions.

The usually given predisposing causes of pellagra are, as follows:

*Seasons, heat, and sun.*—The appearance, or recurrence, of the symptoms of the disease in spring is almost constant, but the seasons, heat, and sun are thought to have only indirect effects in the maturing of corn and development of parasitic growths; the

actinic rays of the sun probably often act as an exciting cause in the production of the erythema.

*Climate* is thought to have no effect beyond the indirect influence in growing and maturing corn and the development of parasites on the grain. But change of climate is beneficial as a means of treatment.

*Sex* seems to exert no influence, though nervous symptoms are said to be more dominant in females. In our experience in the South females have greatly predominated, but this has not been so in other parts of the United States.

*Age.*—The statements are somewhat discordant, but most authors agree that the disease does not occur in infants unless they are fed on spoiled corn. It seems to occur more frequently between the ages of 20 to 40 years. Children are, however, by no means exempt.

*Alcoholism, previous sickness, constitution, hygienic conditions, poverty, venereal excesses, depression, pregnancy, and frequent child bearing.*—These all exert only the indirect influence of lessening resistance. It should be added, however, that several observers believe that alcohol distilled from spoiled corn may contain the pellagrogenous poison. Alcoholism and pellagra are not infrequently associated.

*Other associated diseases.*—It should be noted that such parasitic diseases as anchylostomiasis (uncinariasis) and bilharziosis are frequently present in pellagrins. Malaria, too, is common. These are, however, regarded only as complications, and not as causative agents. They frequently obscure the clinical picture of the disease, however. Babes and Sion think malaria of great importance, and say that

it often prepares the soil for pellagra. This subject has received further discussion elsewhere.

*Nationality and occupation* seem to have no effect. The disease seems limited to certain countries only because of the poor quality of the corn and its consequent readiness to undergo the change described. The poor rural population in Italy are thought to suffer most because they live largely, if not exclusively, on corn and usually of the poorest quality. In the South the disease is much more frequent in the negro in our experience.

*Heredity.*—The disease seems at times hereditary, and the children of generations of pellagrins are frequently feeble in resistance, and of lowered physical vitality, and hence fall easy victims to the disease.

It may be of interest in this connection to add that Bass has reported complement-fixation tests, with lecithin as antigen, in 16 cases of pellagra seen in the United States. His results were: Four of the cases, all positive, were ruled out because of syphilis, malaria or autopsy blood; eight of the remaining twelve gave positive reactions and four negative. The four negative cases were of the severe type; seven of the positive cases were mild or chronic cases; one was severe. He has called attention to the fact that the Wassermann reaction, and its modifications with lipid substance as antigen, have been found in protozoan diseases and not in those caused by bacteria. The hemolytic unit used was 0.2 c. c. sheep corpuscles. The amount of patient's serum used per hemolytic unit was 0.1 c. c. The lecithin



solution was 0.1 c. c. of a 0.3 per cent. solution in equal parts absolute alcohol and salt solution.

Fox has also reported 30 cases tested by the Noguchi modification of the Wassermann reaction. The entire series of cases was tested four times. With one exception, no strongly marked positive reaction was obtained, and in this positive case a complication of syphilis was thought probable. He remarks that if such a sensitive test as that of Noguchi fails to show many positive reactions, it does not seem probable that they will be obtained by the regular Wassermann method. For his technic and details the original paper should be consulted. His conclusions are that cases of pellagra do not often give a positive Wassermann reaction. A positive reaction, when obtained, is generally weak and is easily distinguished from the strong reaction found in syphilis and in many cases of leprosy. The value of the Wassermann test is not affected by the findings in pellagra.]

## CHAPTER V

### CLINICAL STUDY OF PELLAGRA.\*

To give any clear and succinct clinical description of a disease like pellagra is a task beset with no little difficulty. The malady is so protean in its manifestations and often so varied in its evolution as to make a clear and logical description of it by no means easy. Almost all writers and clinicians seem to have been impressed with this fact and hence Lombroso's epigram "There is no disease, only the diseased."

Notwithstanding this, pellagra is a definite morbid entity and remains true to itself and many descriptions of its clinical features have been given by which it can be clearly and definitely recognized.

Most authors, from the time of Frapolli, in an attempt to simplify the matter, have in their descriptions resorted to a more or less artificial division of pellagra into periods or stages, somewhat after the divisions commonly used in describing syphilis. Lombroso, as we shall see later, seemed to regard such a division as unscientific, if not inaccurate; and he preferred rather to speak of types, such as the cerebral, the gastric, the florid and so on, designating each case by its predominating manifestations. By far the majority of authors, however, have resorted to the division into stages. But the division into herpetic or erythematous pellagra, nervous or digestive, may be rejected because such symptoms may all be present simultaneously.

The elder Strambio, one of the very early writers, divided the malady into intermittent, or those having

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\*This chapter is by the translators.



symptoms at one season of the year and remaining entirely well in the intervals; the remittent, or those having acute manifestations at one season without entire recovery in the intervals; and finally the continuous, or grave cases, with constant, severe symptoms.

Roussel, the great French pellagrologist, in his classic work, attempted a more elaborate and more logical division. He divided the malady into three degrees.

A. Pellagra of the first degree, or spasmodic pellagra, corresponding to the intermittent form of Strambio. This condition he subdivided into (a) commencing pellagra, and (b) confirmed pellagra. Here he also included *pellagra sine pellagra*.

B. Pellagra of the second degree or paralytic pellagra, the remittent form of Strambio.

C. Pellagrous cachexia, of which he recognized two forms, (a) with the eruption, or the continuous pellagra of Strambio, and (b) without eruption, being in reality a cachexia consecutive upon its somatic stigmata.

Casenave and Schedel, who wrote in the second quarter of the last century, pertinently say: "The division of pellagra into commencing, confirmed and inveterate, is not a practical one, for pellagra may be beyond hope from its commencement. The expressions period or degree, which convey the idea of certain fixed symptoms and appearances, are not adapted to the description of a disease so capricious as pellagra. The term degree seems to indicate an increasing intensity; while the second or third time

of appearance of the disease may be less severe than the first. When we employ these terms, therefore, we shall use them only as symptoms of a more or less advanced step of the disease; for, like every other disease, pellagra has a beginning, a progress, and a termination."

Among the more modern authors, Babes and Sion speak of (1) a prodromal or pre-erythematous stage, (2) an erythematous stage, with gastrointestinal disturbances, and to a lesser extent general and peripheral nervous symptoms, (3) a stage displaying marked nervous and psychic phenomena, and (4) a stage of general depression and cachexia.

Many authors have thought the division of prodromal, first, second and third stages, being the simplest, is the best; and since any division must to a large extent be arbitrary, it would seem just as well to use the simplest. But the fact remains that the evolution of pellagra in a given case is not so logical as to have one stage succeed another. In a general way, it may be affirmed that the so-called first stage has reference to the gastrointestinal and skin symptoms; the second stage to the cerebro-spinal and psychic phenomena and finally the third stage refers to the cachexia which follows according to the degree of intoxication or the individual's resistance. As a rule, pellagra is a chronic affection and the duration of each stage is indefinite. Furthermore, the line of demarcation is not well defined between the different stages. It is well to recognize that from the start pellagra is a tropho-neurosis. Neurasthenia is an early and an



almost constant symptom and for the clinician this is a fundamental conception of the disease, as will again be emphasized in the discussion of the nervous and mental stigmata of pellagra.

Until the etiology of the disease has been finally determined, we must be content with the clinical summary.

Again, as in beriberi, cases of pellagra have been divided into "dry" and "wet" forms according as the cutaneous lesions remain dry or become edematous and bullous. The latter condition is of much more serious prognostic import. According to Procopiu, Soler recognized this division into dry and wet forms, the former being met with in dry and elevated places and the latter in low and marshy territory. Soler says that wet cases have the abdomen distended, and are pale, cachectic and edematous. The latter form Procopiu regards as associated with malaria. To these conclusions we cannot agree. The wet form seems to arise from a more virulent form of pellagrous intoxication. Whether the wet cases are due to some predisposing or complicating cause—such as malaria, syphilis, tuberculosis, etc., requires further investigation. Likewise the possibility of the influence of some secondary agencies in these cases must not be lost sight of.

It should also be remembered that the disease picture may not be identical in adjoining countries or provinces, to say nothing of different countries or remote States. The disease also presents different characteristics in the same place at different seasons and in different years. The gastro-intestinal type



Plate IX. South Carolina case. Chronic dermatitis showing deep fissures. Also dactylitis and deformities. Probably a complicated case.



may be more marked at one time, to be followed at another season by more striking cerebral or spinal phenomena, and even the type of dermatitis is subject to seasonal variation.

"Pellagra has a course distinguished by pronounced attacks alternating with periodical ameliorations and exacerbations. The exacerbations occur regularly in the spring. During the first attack stomachic and intestinal symptoms with nervous disorders set in, accompanied mostly by an exanthem. In the following attacks the disorders of the nervous system become more predominant and may cause a plurality of symptoms, attended by a development of general cachexia." (Scheube.)

Sandwith says the incubation period of pellagra is perhaps from nine to twelve months' duration. Procopiu thinks this term belongs rather to the infectious diseases and should give place to the prodromal period.

According to Scheube the *prodromal stage* lasts for a longer or a shorter time. For several winters the patient feels languid without cause, and has no inclination for bodily or mental work. Most pellagrins do not pay any attention to the beginning of their malady and only consult the physician when the disease has made some progress. But the skin does not present the first symptom.

Pellagrins often complain of fleeting pains in various parts of the body. This is the neurasthenic stage as recognized by Gregor, who says that when neurasthenic symptoms have lasted for several years without obvious cause, the physician should suspect pel-

lagra. Paresthesias and formications are also indications of a pellagrous intoxication.

The patients complain of a sensation of burning in the mouth and stomach. Examination of the buccal mucosa discloses a general redness, sometimes with vesicles or even superficial ulcerations. The salivary glands are very active, and the secretion may flow involuntarily from the mouth. The saliva is said to be acid. Procopiu considers that this pytalism is not due to the buccal lesions but probably depends upon the action of the poison upon the glands or upon the central nervous system. This stomatitis does not occur in all cases, but is frequent.

For several weeks, sometimes for several months, and in rare instances for a year before the appearance of the erythema, the patients note a progressive weakness, especially of the feet and legs, pressure in the stomach and loss of appetite.

Roussel, according to Babes and Sion, regarded loss of appetite, nausea and gastric disturbances as complications, while he considered dryness of the esophagus, with dysphagia and pyrosis as the first true pellagrous symptoms. These symptoms, as also great hunger, vomiting, cardialgia and diarrhea, Roussel regarded as of nervous origin. In addition other authors note vague fleeting pains in the extremities and back, roaring in the ears, asthenopia, morning tire, often pains in the joints, headache, vertigo, and general debility. Babes notes that there is often, preceding the erythema, a peculiar redness of the lips and tongue, the latter being smooth, slimy or in some cases swollen, trembling and fissured.

We have frequently noted a peculiar injection of the papillae of the tongue, often pigmented, of an intense crimson in the white race and dark or black in the negro. It seems to be commoner in the negro and gives to the tongue a stippled appearance.

In European countries the distinctly pronounced symptoms of pellagra appear in April and May. (Scheube.) In America this is also true, but the most numerous and severe cases seem to occur in May and June, and in September and October. It is also possible that the time incidence may vary in different years. Usually the *first stage* is ushered in by gastro-intestinal disturbances. Loss of appetite, and disgust for food or bulimia appear. Many patients suffer from great thirst, while others have an antipathy for drink. Eructations are common and the chain of symptoms of so-called nervous dyspepsia present themselves. The tongue is coated centrally, but its edges are smooth and slimy. Papillae are pronounced and often injected. Sometimes the epithelium of the tongue is shed and we have the "bald" tongue of Sandwith, sometimes called the "cardinal" tongue. Abdominal distension is common and painful. Diarrhea usually sets in, the patient having ten, twenty or thirty loose stools in twenty-four hours. Dysentery is not infrequent. With the usual paradox of pellagra constipation may be present. Many patients complain of hemorrhoids. Vague nervous phenomena now appear. Insomnia is characteristic. Headache, giddiness, and vertigo are usually complained of, as well as ringing in the ears, pains in the neck and back, a

sensation of constriction and feebleness and uncertainty of movements, especially in the legs. At the height of the attack the tendon reflexes are considerably increased. Psychic phenomena are common; depression of spirits, apparent disturbance of memory, difficulty in thinking and disinclination for bodily or mental exertion. (Scheube.)

With these symptoms usually the characteristic skin manifestation appears. As Sandwith correctly says, the eruption, although the least important of the various symptoms, has given the disease its name and always received an undue amount of attention. Following his observations upon pellagra in the United States, Howard Fox has recently pertinently observed: \* "The name erythema, by which the eruption of pellagra is generally denoted, does not appear to me to be entirely appropriate. It would seem quite proper to use the term erythema for the first stage of the disease, which resembles an ordinary sunburn, and which lasts only a few days. But it seems somewhat anomalous to speak of the entire eruption as an erythema when the erythematous stage is so comparatively insignificant, while the stage of desquamation is so characteristic and of such long duration. An eruption which is called an erythema conveys the idea of affections such as erythema multiforme or the so-called toxic erythemata, which are not as a rule accompanied by desquamation. The general term dermatitis would be a more appropriate name, in my opinion, than ery-

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\*Personal Observation on the Skin Symptoms of Pellagra, Med. Rec., Feb. 5, 1910.

thema for the pellagrous eruption." This dermatitis particularly affects the backs of the hands, the lower third of the forearms, occasionally also the dorsum of the feet; it also appears on the face, neck and upper part of the chest, in fact on those places that are uncovered and exposed to the sunlight. In the case of persons, who whilst laboring go almost naked, such as the fellahs in Egypt, the greater part of the body is affected. (Scheube.)

Brault, in Algiers, Nicholas and Jambon, in France, and more recently E. B. Saunders in South Carolina, have directed attention to a dermatitis occupying the whole vulvar region, as well as the perineal, the anal fold and the internal surfaces of the thighs, which are brought in contact by adduction. Here pressure, as was noted by Sandwith, is clearly an exciting cause of the inflammatory eruption. In many of our cases, the surface of the elbows and to a less extent of the knees is involved for a long while. There is also a tendency for the dermatitis to extend from the elbow down the ulna, sometimes meeting the "gauntlet" coming up from the hand. Here again pressure is a causative factor.

Scheube says: "The skin becomes red and swollen, causing the patient to experience a sensation of tension, itching or burning. Sometimes little blebs and pustules that dry up to scabs develop. After the erythema has subsided for a few weeks, a desquamation of the epidermis in large patches takes place." Rarely this condition does not dry up, but a considerable edema develops, followed by bullae, pustules and even gangrene. These constitute the



"wet" cases, which form one of the most distressing conditions associated with pellagra. Undoubtedly, such cases were not infrequently diagnosed dermatitis exfoliativa, etc., in the United States prior to the recent recognition of pellagra.

By the end of summer or beginning of winter, the condition of patients suffering from first attacks ameliorates. But for a long while the skin of the affected regions remains either pigmented, rough and dry or else appears smooth, shiny and atrophied.

Again following Scheube's classical description of the evolution of pellagra, the illness gradually passes into the *second stage*, which is characterized by serious cerebro-spinal symptoms.

1. *Motor Disturbances.* Severe pains in the back, headache, numbness, cramps and subsults mark the beginning of the second stage. The muscular weakness of the legs becomes more marked. The patient becomes disturbed and distinctly paretic. "The following motor symptoms of irritation are observed: muscular tension and tonic contractions of the upper and lower extremities, which may increase to tetanic rigidity, sometimes also there is tremor of the arms, the head and the tongue; likewise cramps, convulsive jerks and uncontrollable movements of single limbs; exceptionally, also there are pronounced epileptiform fits with loss of consciousness." (Procopiu.) "The gait is either simply paralytic or paralytic-spastic."

2. "*Disturbances of Sensibility.*" The sensibility of the skin is unequal. The sense of touch remains intact, and also the sense of temperature, whilst

much more frequently the sense of pain, particularly in respect to the legs, is diminished. The muscular sense is normal.

"Paresthesia is seen very frequently and in great diversity. The sensations of itching and burning on the trunk and extremities is the most frequent and becomes so intolerable that it drives some patients to commit suicide. There is, moreover, the sensation of formication, subjective sensations of temperature, burning of the eyes, dragging of the neck, sensation of suffocation, a feeling of constriction in the throat and about the chest, a feeling of a band round the body, a sensation of weight in the region of the groins and uterus or testicles.

"The tendon reflexes are mostly increased, frequently to a considerable extent, particularly the knee-jerk; very rarely, however, the patellar tendon reflexes are either weakened or quite absent.

3. "*Disorders of the Organs of Sense.* Occasionally weakness of vision, hemeralopia, diplopia, muscae volitantes and photophobia are observed.

"After repeated attacks the skin becomes of a brown hue and appears smooth, dry and thin: it also loses its elasticity, so that it may be lifted up in folds, which remain in position. The nails are very rarely found normal in pellagra patients, being mostly clubbed, ridged, grooved, split, very thin, necrotic or overgrown with skin." (Scheube.)

After repeated attacks or by reason of their severity the patient passes to the *third or cachectic* stage. This is really the terminal stage and is chiefly characterized by cachexia. The symptoms



already described do not give place to new ones, but, on the contrary, they are present and aggravated. The cachexia now, however, stands boldly in the foreground, with dementia, paralysis, and other cerebro-spinal phenomena still prominent in the picture.

There is an increasing marasmus, with marked anemia, atrophy of subcutaneous fat and musculature, and a lack of resistance against intercurrent diseases. In addition there are great muscular feebleness, perhaps paralyses, including the bladder, and an uncontrollable, painless, serous diarrhea. Death follows, with the signs of heart weakness, and its consequences, edema, and effusions; or some intercurrent disease, such as acute tuberculosis of the lungs, which is common at this period, or septicemia following decubitus, may close the scene.

Nearly a century ago, Brière de Boismont concluded his studies of pellagra with this among other corrolaries: "Pellagra is sometimes a primary irritation of the digestive organs complicated with lesions of the nervous and cutaneous systems. Sometimes a malady of innervation with secondary lesions of the digestive functions. In some cases the nervous system alone is attacked. The cutaneous stigmata which may be wanting are not a criterion of the severity of the other symptoms and may disappear before the recovery of the patient. These stigmata are of secondary importance, and that, too, in all cases.

"The three stages are not as absolutely distinct as some claim. The second, which is usually fatal

unless improvement soon begins, may remain stationary for several years. The third is incurable. Change of location and manner of life exert a happy effect upon pellagrins."

#### FORMS OF PELLAGRA.

Many forms have been described and various divisions made. One or more symptoms may dominate the picture.

It will be seen that Lombroso speaks of the different "forms" of experimental pellagra in dogs as anemic, spasmodic and cerebral, and prefers these terms rather than that of pellagra in general; and furthermore that he regards it as more didactic than scientific to make divisions into first and second stages (page 102). In man, Lombroso recognizes such types as the cerebral, ganglionic, spinal, spastic, tabetic, atrophic, gastric, cutaneous, sexual and finally the fulminating, florid or tetanic types (page 183). Lombroso also uses the term period. But several times (pp. 210-214, 227-229) Marie refers to stages or periods, and on page 223 to confirmed pellagra, thus showing how these terms have become engrafted into descriptions of the disease and how difficult it is consistently to avoid using them.

Most of the terms used by Lombroso are self-explanatory. Besides these we have also *pellagra sine pellagra* and typhoid pellagra (*typhus pellagrosus*). By *pellagra sine pellagra*, of course, is meant the existence of gastro-intestinal and nervous symptoms with the absence of the dermatitis. The existence of this type is denied by some writers. (Gregor.)



Such a condition, or, in fact, several pellagrous conditions without the dermatitis are recognized by different authors. The commonest form is that of a persistent diarrhea with the nervous and mental phenomena of the disease. E. J. Wood, after former skepticism regarding the condition, now seems inclined to consider it as a terminal phase of pellagra.\*

No doubt some cases will be called *pellagra sine pellagra* because the history of the eruption cannot be obtained, although it has previously existed and disappeared. This is particularly true of insane cases, and in these the most careful search should be made for the relics of the skin stigmata of pellagra. Such examinations often clear up the situation.

The term typhoid pellagra (*typhus pellagrosus*) has been employed by nearly all writers upon the disease. According to Scheube, it is an acute aggravation of all the symptoms, more especially the mental: "The whole muscular system is in a condition either of rigidity or intense tonic contraction. The head is buried in the pillows and at times convulsively moved. On spontaneous movement of the limbs a perceptible trembling and indications of incoordination are made manifest, and tremors and fibrillar contractions are seen in the face from time to time. The speech is drawling, tremulous and often exhibits a nasal twang. Frequently there are hyperesthesia and heightened reflex excitability, the tendon reflexes in particular being always increased."

The temperature is frequently high, but the condition has been observed by both Italian and German

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\*Trans. Tri-State Med. Assoc., 1909, p. 446.

writers without elevation of temperature. It is hardly necessary to say that the condition has no relation to typhoid or enteric fever, although Procopiu asserts that he has twice seen pellagrins develop true enteric fever, and the same observation has been twice made by J. J. Watson in this country.

Furthermore, Procopiu considers typhoid pellagra as a complication which may sometimes be due to Eberth's bacillus, and then we have an association of of the two diseases. He adds that the condition is most frequently caused by different kinds of microbes, which in the intestines of healthy persons have no pathogenic action, but end by overwhelming the cachetic pellagrin whose natural resistance is greatly reduced.

Tanzi says: "This (*i. e.* typhoid pellagra) is a very serious incident in the course of pellagra, which occurs usually only in extremely inveterate cases several years after the onset of the disease.

"The course of pellagrous typhoid is always short: there is no cutaneous rash; the abdominal symptoms are accompanied by opisthotonus, epileptiform attacks; rigidity of the legs, and constant delirium, which indicate the special origin. Sometimes there are added nephritis and uremia, with ammoniacal odor of the perspiration, but the urine is fairly abundant, and although it contains casts, is almost devoid of albumin. Pellagrous typhoid is a fatal complication which runs its course in, at most, one or two weeks."

*Resumé.* The above is an outline picture of pellagra as usually seen by the clinician, but the triad of symptoms upon which the diagnosis is usually

based demands, it seems to us, separate and further analysis. The descriptions that follow are based largely upon the studies of Roussel, Procopiu, Merk and Gregor. So far as possible credit is given for separate quotations, but it has not been practicable in every instance.

*Digestive Symptoms.*—A majority of pellagrins are dyspeptic, and the dyspepsia often persists when the other symptoms have disappeared. Ordinarily it is a flatulent and painful dyspepsia. Thus during winter when the patients do not show the characteristic stigmata of pellagra, dyspepsia and gastralgia alone persist.

In regions where pellagra reigns one may often see persons for two or three years before presenting the disease picture of pellagra suffer from dyspepsia characterized by pyrosis, flatulence, eructations and painful digestion. This dyspepsia must be due to the same cause as pellagra and these persons subject to a form of *pellagra sine pellagra*, that is, pellagra without the exanthem. Roussel said with reason: "The expression *pellagra sine pellagra* can only be applied to a temporary absence of the cutaneous eruption either at the beginning or during the course of the malady." But this absence may be of long duration when the only manifestation of the pellagrous poisoning consists in digestive troubles.

Strambio first admitted *pellagra sine pellagra*. Naturally it is difficult always to recognize the nature of these dyspepsias and gastralgias, but in considering their relationship to the dietary and the appearance of the dyspepsia in the spring, one may suspect its origin and the removal of the cause may of itself lead to the cure. (Procopiu.)

Gastralgia is a later symptom, often developing after the others have disappeared. What has been said about the dyspepsia applies equally to the gastralgia. These gastralgias have some resemblance to the gastric crises of tabes. They supervene sometimes in paroxysms and it is not rare for them to cause gastric intolerance. They last several days and generally have no relation to the taking of food.

The gastric juice is often less acid in pellagrins. The hydrochloric acid is diminished. This fact proves that the sensation of burning referred by patients to the stomach and which rises towards the esophagus is not due to the acidity of the secretions but to other causes. It is probably a purely nervous sensation, or one depending upon lesions of the mucosa, analogous to the erythema. This last hypothesis appears more probable for the sensation of burning of the mouth is always associated with hyperemia of the mucosa and with other lesions which are found in the stomatitis of pellagra. (Procopiu.)

According to Roussel constipation is not infrequent, especially in the earlier stage in pellagra, but it may alternate with diarrhea. In the first stage also sudden attacks of diarrhea occur, having the characters of spasmodic phenomena. Strambio distinguished two kinds of diarrhea: the one, a dysentery characterized by frequent, colicky and muco-sanguinolent stools; the other more common and characterized by watery discharges, frequency and great obstinacy. The dysenteric form is more common in the earlier stage, but the serous or aqueous diarrhea belongs to the later and progressive stage, and is an important factor in producing the cachexia.



*The Pellagrous Dermatitis.* For the following descriptions we are indebted largely to the works of Procopiu and Merk.

The erythema appears early, usually at the beginning of spring, but there are great variations as to the time of its appearance. We have seen that the dermatitis is usually preceded by prodromal symptoms, specially of the digestive system.

Most authors claim that the skin lesions affect only the parts of the body exposed to the sun. Merk says that it was Raymond who first spoiled the vicious logical circle: "The sun produces the pellagra erythema, because the pellagra erythema is only on the parts exposed to the sun." Some writers, Calderini and Socor, have described the eruption upon unexposed parts. The influence of the sun is not to be questioned, but it is secondary. Bouchard has shown that it is the chemical or violet rays that exercise this action. But the observations of Calderini and Socor prove that the essential cause of the erythema is within the human organism. Procopiu thinks that probably the exanthem is due to the elimination of the poison by the skin. J. D. Long ascribes it to pressure by pellagrous deposits upon the spinal nerves at their foramina of exit. The assertion of Strambio, Bouchard and others that the cutaneous symptoms may be avoided by keeping in the shade is not correct. For, granting that the exanthem may thus develop more slowly, the skin is none the less affected in the shade, but sunlight intensifies the eruption, and it is not to be denied that the rays of the sun are thus an exciting cause of the skin lesions, for the eruption appears upon

unusual sites when the sun's rays penetrate through a tear in the clothing.

*General Character.* The dermatitis of pellagra is characteristic and pathognomonic. When it is lacking, the diagnosis is very difficult, especially in a region where pellagra is little known. The lesions begin as an erythema upon the dorsal surface of the hands accompanied by pruritus and burning. Symmetry of the skin stigmata of pellagra is an essential feature of the disease. The skin is slightly edematous. In some patients several days afterwards, blebs appear, which may run together and form bullae, containing a serous or sero-sanguinolent fluid, which escapes as the bullae burst. When the edema disappears the epidermis desquamates and falls off in the form of little grayish scales. After this desquamation the sensations which accompany the lesions improve or disappear.

In other cases, the epidermis, after having presented the characteristic redness, takes on a brownish color, separates and falls off in the form of dry scales without forming blebs. Sometimes desquamation of the epidermis is observed without preliminary redness. In these cases after the shedding of the superficial epidermis, the integument remains thin, smooth and a deep red.

Following his careful study of pellagra in the United States, James Nevins Hyde has said:\* "The hue of the exanthem differs according to the color scheme of the subject and the length of time during which it has existed. At first the color is a dull red, which has been likened to the appearance of the skin after a common sunburn; yet it is rare that the

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\*Am. Jour. Med. Sci., Jan., 1910.

pinkish hue produced by the rays of the sun in the skin of a blond subject is precisely imitated. The pellagrous erythema at the outset, generally fading temporarily under pressure, is more reddish than pinkish, displayed at times with discrete macules, which speedily fuse and produce, on the backs of the hands, for example, a uniformly, smooth, reddened and distinctly outlined area, suggesting the appearance of a glove covering the back of the hand. . . . As the evolution of the erythema advances, the color deepens, refuses to disappear under pressure, and at its height attains a reddish-brown, chocolate or plum-colored shade, described as 'livid bluish,' a tint at times suggesting that of sepia. The first eruptive symptoms may disappear in a fortnight, with epidermic exfoliation in light flakes, leaving behind a pigmentation differing according to the severity of the precedent engorgement."

The dermatitis develops in the same fashion in other parts of the body. Upon the face the scales are thicker and larger. Pustules have been observed. Here there is probably an association with acne, for this pustulous erythema, says Procopiu, is met with only upon the face. Pustulous inflammation in other parts—the perianal and perineal regions and the backs of the hands—is probably due to secondary infection with the common bacteria of suppuration.

After several relapses, the exfoliation takes place in quite thick lamellae. When the malady reaches the second stage, the dermatitis becomes hard, rough, cracked, blackish, and brittle. The epidermis of the fingers thickens, blackens and becomes indu-



Plate X. South Carolina case. Exfoliating dermatitis of feet, the lesions being slightly "wet."



rated. The articular folds appear deeper. Kaposi says that at this period the skin is of a reddish blue or a bronzed-brown, with the epidermis thin, satiny-like and excessively sensitive. Procopiu has found it blackish, never reddish blue, and the sensibility has appeared to him somewhat diminished. The explanation of this difference of opinion as to color indicates that pellagra assumes different color schemes in different localities.

The elasticity of the skin disappears after several attacks. Painful fissures develop in the palms of the hands. Roussel erred in asserting that these fissures are always foreign to pellagra. In South Carolina at times, deep fissures develop upon the fingers, especially the index finger. These fissures appear after several relapses. The appearances of the integument in pellagrins has been compared with the skin of the goose, hence it is sometimes called "goose skin."

It is not rare to see small superficial ulcerations after the shedding of the epidermis, especially upon the extremities.

When the malady is far advanced, the skin becomes hard, dryer, cracked, covered with thicker scales, and even with blackish crusts which arise from little hemorrhages occurring under the scales.

Often instead of the erythema, after the falling of the scales and crusts, ecchymotic spots appear, which Fanzago confounded with the red spots which follow the desquamation.

In patients at the State Hospital, Columbia, S. C., we have seen ecchymotic spots under the epidermis of the palms and soles, varying in size from a pea to the thumb nail. They sometimes suggest the appearance of sub-epidermal freckles. Similar stigmata have been observed by Samuel Stern in patients at the Philadelphia Hospital for the Insane. E. B. Saunders has noted: "The vulvar mucous membrane often shows the same 'stippled' appearance as the tongue. Small hemorrhages, such as are observed under the epidermis of the palms and soles have been seen under the vaginal and vulvar mucous membrane and adjacent skin." Like the injected papillae of the tongue, they seem to be hemorrhagic and suggest a scorbutic taint. But that they belong to the disease-picture of pellagra admits of no doubt. The nails are fragile, brittle, and of a grayish color. The dermatitis, as does the disease, evolves in a periodic manner; it begins in the spring and disappears at the end of several months to reappear the following year at the same time.

Sometimes the erythema is almost the only symptom which the patient presents; other symptoms are wanting or only slightly appreciable. But these cases are rare; much oftener slight or severe digestive troubles exist, their absence being exceptional.

*Localization.* The usual sites of the dermatitis are, according to Procopiu, the face, neck and dorsal surfaces of the hands and feet. Rarely it is observed in other places.

Among the common localizations described by Merk are: the dorsal surfaces of the hands and feet,

the face, the neck and sternum (the Casàl necklace and cravat).

The backs of the hands are the most frequent sites of the exanthem. It may be confined to the back of the hands or extend up the arm forming the "glove" or "gauntlet" of pellagra. The symmetry of these lesions is one of the striking characteristics of the malady. The cross line is two or three fingers above the wrist, or usually confined to the lower third of the forearm. The pellagra zone does not include all the weather tanned area. The more violent the eruption, the higher can the erythema zone extend, although this is not a fixed rule. Raymond thought that the dermatitis spared the last two phalanges. This is emphatically not so in South Carolina, the fingers being involved to the tips even on the palmar side. J. J. Watson, as quoted by Hyde, has pointed out a characteristic extension of the pellagrous eruption on the hands to the flexor surface, beginning on the radial border, and reaching toward the ulna by an oblique line forming an irregularly outlined triangular patch, its base at the radius, its apex near the ulnocarpal articulation.

As to the feet, Merk says the general type fixes its proximal limit by a straight line passing directly across the ankle in the maleolar region, in fact the maleoli are, as a rule, included in the disease zone. The heel remains free. Distally the eruption ends at the toes or on the backs of the great toes. Usually the back of the great toe is most, and of the small toe the least affected. In Egypt and the United States the dermatitis sometimes extends up the front and back of the leg, forming a "boot."



Upon the face the lesions appear with surprising symmetry. Merk recognizes a diffuse and a spotted type. In the weakest grades of the spotted type only the region of the sides of the nose is affected. Then, in order of frequency, the rest of the nose, the forehead, the cheeks, the chin, the lips, more rarely the eyelids or the ears. The spots are the size of a small coin and round, in other cases they produce wreath-like figures, or have serpiginous or sinuate boundary lines, such as in general belong to the erythemata.

In South Carolina in severe cases, especially in negroes, it is not unusual for the dermatitis upon the face and nose to assume the "butterfly" appearance common in lupus erythematosus. The whole muco-cutaneous junction is occasionally involved in severe cases, the inflammation having a wider area at the angles of the mouth.

The diffuse type on the forehead comes close to the hair, but still always leaves a narrow border of sound skin between the hair and the erythema. The dermatitis is most accentuated upon the glabella, forehead, nose and cheeks. The erythema upon the face may be so slight as to be overlooked. Casàl did not note it and Merk gives Frapolli the honor of first directing attention to it. In European countries it is the women and children whose faces are most affected, but in Mexico Vales asserts that the faces of men are most frequently involved. This facial dermatitis has been called a "mask" by Italian authors, and it never appears independently of lesions upon the hands and elsewhere.

Casàl's "necklace" extends as a tolerably broad band or collar entirely around the neck, its upper border reaching somewhat below the hair line to the Adam's apple in front; the lower border beginning under the vertebra prominens and extending in front to the edge of the manubrium. Sometimes the band is only as wide as the finger. Again it can be incomplete, leaving the vertebral region or that of Adam's apple free, or only the vertebral region may be affected. Symmetry of lesions is especially noted in incomplete bands. In many cases the necklace has a front continuation or broad "cravat," extending from the manubrium over the sternum to the level of the nipples, ending pointedly or square. Men, women and children have the necklace. Merk has seen the cravat only in men, but Prócopiu pictures it in a pellagrous boy. We have under observation a young negro woman severely affected who presents the Casàl collar, and a squarish cravat extending four inches below the manubrium. This eruption is always accompanied by the characteristic dermatitis elsewhere.

According to Merk, it is only within recent years—that is, since the skin lesions have not been regarded as due entirely to the sun—that atypical localizations of the dermatitis have been recognized. Merk says Deiacò was the first to describe the dermatitis upon the external genitals of females. Stephanowics puts in a claim of priority over Deiacò. Pellagrous vulvitis and vaginitis have been long recognized. Among the atypical lesions mentioned by Merk, are those upon the shoulders, perianal region, elbows, forearms, knees and scrotum.

Lesions typically located, says Merk, may be found in the same case with atypical ones, thus rendering the diagnosis easier. But atypical lesions may appear entirely alone, though they have not been recorded as observed in the erythematous stage.

In South Carolina, especially among the negro pellagrins, dermatitis of the elbow is very common and to a somewhat less extent the knees are symmetrically involved. In fact, in doubtful cases involvement of the elbows is an aid to diagnosis. The relics of the dermatitis upon the elbows should always be sought for in doubtful cases and in cases of *pellagra sine pellagra*.

Sometimes the exanthem covers the larger portion of the body but rarely it is universal. Such cases weaken the solar theory. Again, it affects only the backs of the hands. It is entirely absent oftener than one would suppose. There are patients who, two or three years before developing the characteristic dermatitis, suffer from gastralgia and diarrhea, especially in the spring. With others the outbreak of the exanthem arises from unusual causes, such as typhoid fever with Eberth's bacillus. Strambio, about 1790, observed that gestation gave occasion for the eruption of pellagra, and in this country E. B. Saunders has directed attention to the fact that latent pellagra frequently develops the characteristic skin stigmata after a surgical or gynecological operation which may have been performed for the removal of nervous or other symptoms. The healing of pellagrous skin lesions is usually centrifugal, that is, the line of demarcation may remain

actively inflamed, after the center of the lesion has desquamated. This dark zone or fringe frequently persists after other signs of pellagra have disappeared and should be carefully looked for in cases of *pellagra sine pellagra*.

J. J. Watson, of Columbia, S. C., has directed our attention to a condition which he has observed several times on the hands of patients who have suffered from a very severe pellagrous dermatitis. In addition to the usual glistening and atrophic appearance of the dorsa of the hands at the site of the eruption there persists for a long time an apparent vasomotor paresis, the hands assuming a cyanotic hue when dependent, but otherwise being red like a goose's foot. Rarely there has been noted a dermatitis of such severity as to produce a teno-synovitis with subsequent restricted movement in the fingers.

It is by no means uncommon in South Carolina for the palms and soles to be almost as severely involved with the pellagrous inflammation as are the dorsa. While we have not seen them in the erythematous stage, we have frequently observed them subsequently when thickened, indurated, blackened and fissured. The subepidermal freckles have already been mentioned. The palms and soles exfoliate synchronously with the dorsa. The soles appear in some cases to be more pigmented. In wet cases the activity of the inflammatory process often manifests itself first by a hemorrhagic zone at the line of juncture of the dorsal epidermis with the thick sole of the foot. This inflammation proceeds with much

activity and soon becomes bullous and later purulent. When the bullae burst the skin peels off leaving a large denuded area of corium. Such cases as these often involve the entire surface of both feet and hands and show a marked tendency to become gangrenous. Other unusual localizations are upon the abdomen, the shoulder-blades and buttocks, and in wet cases on the inner side of the thighs from the groin nearly to the knee, the vulva, and over the trochanters. In fact, as compared with European pellagra, the American type of the disease suggests a more active and virulent form of intoxication. This view is borne out by the frequency of the acute type and the greater mortality of the disease. In brief the type of pellagra now prevalent in the United States is more suggestive of the Italian disease in the elder Strambio's time.

#### THE NERVOUS AND MENTAL SYMPTOMS OF PELLAGRA.

The association of nervous and mental phenomena with pellagra is so important as to require separate consideration. In Italy it has been variously estimated that from four to ten per cent. of pellagrins become insane. It is now well established that this relationship is that of direct cause and effect and not an accident or coincidence.

In the United States up to the present time such statistics upon pellagra as we have come largely from hospitals for the insane and it is impossible to give the ratio of sane to insane pellagrins.

It has long been recognized that the nervous and mental condition of pellagrins undergoes an early

modification. This condition may be ill-defined or show itself by a greater psychic excitability in which a slight insult or threatened danger completely carries them away, thus indicating a lowering of inhibitory power. Again the patient may become hypochondriacal or neurasthenic.

Gregor believes that the first attack of pellagra is more likely to be accompanied by neurasthenia, and that this condition commonly precedes the development of the pellagrous psychoses. He recognizes among the leading neurasthenic subjective symptoms: "Headache, pain in the gastric region, vertigo, paresthesias, lassitude, mental depression, a sense of unrest and anxiety, which may be raised to a phobia, as well as ill-defined apprehensions. There is also a sense of bodily and mental incapacity, and of illness. Their conduct is normal, and the intellect may be unimpaired, but they are incapable of mental and physical exertion. The process of association is distinctly disturbed, the simplest question being answered only after prolonged hesitation. With depression of spirits hypochondriac notions may develop. In some cases there is slight motor unrest, but as a rule these patients labor under motor impediment and sink gradually into a condition of apathy and resigned inactivity."

Upon this neurasthenic basis Gregor has seen develop distinct psychoses; such as acute confusional insanity including stupor, hallucinosis, acute delirium, and katatonia, as well as anxiety psychosis, and manic-depressive insanity. All these conditions he analyzes at length making it appear that in indi-

viduals attacked by pellagra, various psychoses may develop.

Lombroso at one time thought the insanity of pellagra was as a rule of an ill-defined, contradictory character, like that of old age or anemia, and that if it approached a type it was rather that of chronic mania and dementia.

Tanzi is of the opinion that "the first attack of insanity occurs after pellagra has existed for some years and has already given rise to dermatitis and diarrhea and has remitted from time to time. In other words, that the pellagrous lunatic is as a rule a chronic sufferer from pellagra. But whilst the pellagra, although chronic, continues to run an intermittent course, the mental disturbances associated with it have the characters of an amentia," (acute confusional insanity). Furthermore, Tanzi regards "the insanity of pellagra as something different from common melancholia or from ordinary mania. It is also something more than simple amentia. We may regard it as the combination of two distinct clinical pictures, namely, that of amentia in the first attacks and that of dementia in the later and progressive phases, marked by chronic and incurable cachexia. It is an intermittent and progressive amentia, which if not cured or if not early fatal, terminates in dementia." Or, according to Régis, it may end in chronic mental confusion or in pellagrous pseudo-general paralysis.

Following upon a more or less prolonged attack of neurasthenia the patients may thus pass into a state of stupor, tending to remissions and marked by deep

depression and a vivid sense of insufficiency. (Gregor.) In this manner the several types of pellagrous psychoses ordinarily develop.

Among the various nervous diseases that have been reported as resulting from pellagra may be mentioned neurasthenia, hypochondria, neuralgia, chorea, sciatica, polyneuritis, meningitis, myelitis, "epilepsy" and "tetanus." Neusser claims to have seen amyotrophic lateral sclerosis. Bassoe, of the Illinois pellagra commission, according to Hyde, after careful neurological examination of nineteen cases, divided them into three groups: those with probable degeneration of the pyramidal tracts; those with degeneration of the posterior columns and those with combined degenerations. These clinical results are largely confirmed by the pathological findings. (Bowen and Towle.)

The older writers recognized acute mania, acute melancholia, acute delirium, chronic mania, chronic melancholia, pseudo-general paralysis and terminal dementia. Later writers (Gregor) describe: acute confusional insanity (including stupor, hallucinosis, acute delirium and katatonia) anxiety psychosis and the manic-depressive group, besides several forms of dementia, including paresis.

Antonini, Tanzi and Finzi agree that the type of the pellagrous psychosis is amentia, or acute confusional insanity. Vedrani opposes this view, maintaining that the psychosis of pellagra takes usually its course without serious disturbance of orientation and reason. Warnock and Aubert assume especially close relations between pellagra and melancholia.



Baillarger held that the psychoses of pellagra are polymorphic, including meningitis, mania, melancholia, etc., and even general paralysis. Zletarovic agrees to this, but says he never saw mania develop in a case of pellagra. (Gregor.)

Many differences of opinion among writers no doubt arise from the fact that they have studied different expressions of the pellagrous intoxication.

The effort has been made to classify the mental phenomena of pellagra as chronic and acute. Following Bianchi's description, we may say that in the chronic form, the patient shows "general depression, melancholia, confusion, slow dementia, paresthesias and ataxic gait. Contractures and subsulti are absent, although in most cases the reflexes are exaggerated. In the acute form, there is elevation of temperature, intense neuro-muscular excitement, subsulti, contractures, muscular rigidity, exaggerated reflexes, and confusion with episodes of exaltation. There are numerous intermediate forms in which we observe a great variety of psychic phenomena, and also alternations of excitement and depression. Phases of remission and of apparent recovery are observed, especially at certain seasons."

Procopiu says, "the acute form is more frequent when the pellagra is associated with alcoholism, then this form presents the characters of delirium tremens. The acute form often manifests itself in the course of the chronic form, but it can also begin in the state of apparent health." It is highly probable that the acute form of pellagra described by writers is frequently an acute collapse delirium.

*Spinal Disturbances.* Gregor verifies Toninini's observations upon the spinal symptoms of pellagra. These are: Increase of the tendon reflexes, increase of mechanical muscular excitation, tremor of the fingers, rigidities and spasms of the leg muscles, spastic gait, diminution of the tactile, thermal and farado-cutaneous sensibility, paresthesias, ataxia of the lower, and in rare cases, of the upper extremities, and Romberg's symptom. Also muscular spasms: tonic spasms being present in patients in the terminal stage of pellagra, but clonic spasms are also observed and these without the other symptoms of typhoid pellagra. Paresis of the lower facial muscle was also observed.

There is also a diversity of opinion as to the grouping of the pellagrous psychoses. Bianchi and Tanzi classify them with the toxic group, that is, with the insanities from alcohol, morphine, cocaine, etc. Bucknill and Tuke place them under the same heading, while Régis classifies them with the psychopathies of the exo-intoxications and Mongeri, under the infective psychoses, between post-influenzal insanity and Korsakoff's disease. Gregor thinks some of his cases might come under the infective-exhaustive group, but he admits that the depression of pellagra is not dependent upon exhaustion, since it occurs also in well-nourished cases and in favorable conditions of life. The term amentia of continental writers evidently includes a large proportion of these cases, for clinically they fall under an acute confusional insanity, in many of its phases. This classification is further justified by the presence

in many cases of peripheral anesthesia, as emphasized by Stoddart as occurring in this condition.

As Gregor wisely remarks: The many-sidedness of the disease picture explains the view that all forms of mental disturbances may occur in pellagra. Hallucinations and disturbances of orientation occur episodically in the disease.

*Pellagrous Dementia.* For the chronic forms, dementia is the common termination, but it may be complicated by paralysis or tuberculosis. Dementia following pellagra shows, according to Gregor, different forms. One form develops an almost complete disappearance of mental activity, which justifies the name "paralytic." But a milder degree of dementia characterizes the larger number of cases. They are oriented, usually well behaved, but dull and show a lack of self-restraint, with a tendency to break out into violent passion and impulsive actions.

A simultaneously existing alcoholism has a modifying influence upon the disease picture. Furthermore, in many individuals the pellagrous mental disturbance does not appear until old age, when it brings about a precocious senile dementia. There is also a distinct pellagrous dementia, like paresis, marked with somatic changes.

From our observation and study of the subject in America it appears to us that while depression (melancholia), stupor and mutism are the ordinary psychic expressions of the pellagrous intoxication, yet excitement (mania, exaltation) occurs under different conditions. *First*, we may have temporary episodes of excitement lasting only a few hours or a

few days; *second*, an acute, collapse delirium may occur at any stage of the malady and usually terminates in death in from one to two weeks. It may even be an initial delirium. (This is not uncommon in the United States, and it is sometimes called acute pellagra); *third*, the typhoid pellagra (typhus pellagrosus) which occurs as a terminal phase of chronic pellagra. It is rare in Italy and far from frequent in the United States.

Strictly there appears to be no mental symptom-complex characteristic of pellagra, but pellagra may act as the exciting cause of several different nervous and mental states. These are: neurasthenia, polyneuritis, meningitis, epilepsy, acute confusional insanity (including stupor, hallucinosis, collapse delirium, and katatonia), anxiety psychosis, the manic-depressive group, pellagrous pseudo-general paralysis and several other forms of dementia.

It is not unlikely that the mental symptoms of pellagra may differ by seasons, or in different countries and in different parts of the same country, just as, broadly speaking, do the physical signs and symptoms of the disease.

The tendency of pellagrins to suicide has been dwelt upon from the time of Strambio by many writers and observers. Our experience in America is beginning to teach us how painfully true this observation is.

In conclusion, the protean and often paradoxical expressions of this strange malady may again be emphasized, and the clinician is warned to be on the alert for many unexpected nervous and mental phenomena when dealing with pellagra.

## CHAPTER VI

### GENERALIZATIONS—CHIEF FORMS OF PELLAGRA.

#### SIGNS AND SYMPTOMS.

There is a curious saying heard among the poor pellagrins of Venetia which shows that a long and unhappy experience has made the people familiar with the varied manifestations of the malady. This is the saying:

Pellagra can give rise to seven kinds of ills:

- (1) It drives one crazy.
- (2) It drives one into the water.
- (3) It draws one backwards.
- (4) It makes one walk bent.
- (5) It gives one vertigo.
- (6) It gives one ravenous hunger.
- Or (7) It causes rashes on the skin.

[Sandwith says he has often seen all these varieties in Cairo, though the second and third are the most rare and the fourth is not common. We, too, have seen all kinds in this country, though the second and third are rare in our experience, and the fifth, while fairly common, is not of the severity usually described in Italy. Furthermore, Babes and Sion, in commenting upon this subject, say: "It is true that a popular proverb speaks of different kinds of pellagra, but they do not stand the test of scientific criticism."]

There are pellagrins in whom there are no disorders of the skin or of the digestive organs, and who suffer most from disturbances of the motor



**Plate XI. South Carolina case. Dermatitis of face, neck, elbows, hands and knees. Courtesy of Dr. J. J. Watson.**



system (perhaps only a continuous vertigo) and from a general debility.

There are those in whom the phenomena consist in grave psychic alterations and changes in motility and sensibility, such as various hyperesthesias—cerebral, ganglionic or spinal pellagra.

There are others distinguished by a rapid, extraordinary emaciation—atrophic pellagra. Then there is the gastric form with anorexia, indigestion, diarrhea or constipation or voracious appetite; and the cutaneous form, with discoloration of the entire skin, with erythema, furunculosis or herpes. There is one type with unusual sexual excitement. Worst of all and fortunately rare there is the form with a fulminating course and this is called florid, or better, tetanic pellagra. And in experimental animals we see analogues of these various types.

#### LOCAL CHARACTERISTICS OF PELLAGRA.

It is a singular fact that among 600 pellagrins observed it was found that many of the symptoms of the disease which were common in one locality were totally absent in others.

In the district of Pavia the cases of contractures and of mutism are numerous; but in the district of Verona pupillary anomalies prevail. In the latter district pellagra (which the people call pelandria or salso) is not synonymous with insanity as it is in the districts of Pavia, Cremona and Brescia. The salty taste in the mouth is met with more frequently in the pellagrins of Venetia and of south Tyrol; still, in Lombardy this symptom was very frequently observed in the time of Strambio. In



Lombardy now one observes rather pain in the back, frequent dilatations of the cutaneous capillaries, but rarely scurvy. In the district of Triest fewer insane pellagrins are met with, but a larger number of cases of albuminuria and of phthisis combined with pellagra. One can thus understand how the old Italian physicians could confound pellagra with phthisis. At Mantua that which strikes one is the cranial anomalies, which do not exist in other districts (possible ethnic influences).

In the region around Milan the pellagrins have frequent epileptiform attacks, whereas they are rare in the district of Pavia and are never met with in the Tyrol.

The most frequent complication of pellagra in the province of Reggio is scurvy; in Tuscany pterygium is common.

The observations noted in the various localities and circumstances, from the ethnic as well as the geographic and climatic points of view, ought to be carefully considered and arranged; the different kinds of corn, its modes of preparation, exert an influence, as has been seen, as well as the climatic, and racial factors. It is certain that in a population with a disturbed sympathetic system cases of pellagra will be accompanied by vascular dilatation and pupillary derangements. A population predisposed by a constant malaria to leucemia and dysentery will be more easily affected by pellagrous diarrhea and anemia.

Cipriani had already found local differences in the symptoms of pellagra: In the district of

Mugella the cases were slow and intermittent in their course, rarely accompanied by erythema. In Romagna and Tuscany the course of the disease was more violent and fatal, and the erythema more intense. Roussel noted as rare the tendency to suicide in the Landes, while at Cannes such cases were frequent. In the district of Laragna cases of night blindness are numerous; in Spain coarse tremor of the head is common. A distinguished Italian observer of pellagra, Soler, compares the pellagra of mountains with that of the plains—the one showing the dry form of erythema, the other the wet. It does not seem impossible that a purer atmosphere may retard the development of the poisoning. Thus, to this cause is attributed several cases of semi-immunity observed in mountainous regions where individuals of a pellagrous family present a very mild type of the disease. Cases of pellagra observed on the southern slope of Monte-Baldo were not severe; it seems, therefore, that locality plays its role. Thus, possibly, Strambio's criticism of Soler in this connection would seem unjust.

Pellagra varies not merely from one region to another but also from one individual to another, just as one or the other organ offers less resistance; and in this lies the reason why there is no other disease of which one can say with more of truth that "There is no disease, only the diseased." Something analogous is found in many intoxications and infections, which, although presenting many specific symptoms, can present often very diverse lesions. Just as the malarial infection, for example, displays

gastric, tetanic and other forms, so similar variations are observed in the phenomena of poisoning by corn.

While in the course of pellagra we have an entire series of cardinal symptoms of which pigmentation of the skin is to be especially noted and the importance of which will be shown in the section on pathologic anatomy, still the skin of the pellagrous is not merely erythematous, pigmented and desquamating; it also bears eczematous and herpetic efflorescences, which seem to have some influence on the progress of the malady. In many districts, however, numerous variations and anomalies are observed in the respect just mentioned and in other respects. The importance of the genito-urinary symptoms is also to be noted. In individuals poisoned by corn observation shows frequent *ardor urinae*, with increased density of the urine, and not infrequently dysuria. More interesting still are the results of urinary analysis. In certain of these pathologic states the urine is increased neither in quantity nor in density, but, on the contrary, is often diminished; its acidity is lessened and it may be neutral or alkaline. In all cases there is a diminution of urea, of the phosphates and of the chlorides in spite of good nutrition. [In the United States the presence of indican is very common.]

The diminution of muscular force is not a universal symptom, but agrees, indeed, with the majority of the observations on poisoning by corn, as in many other kinds of poisoning.

More specific still, so to speak, are the disorders of the sensibility—pruritus, paresthesia; above all, sensations of heat; the disorders of the special visual sense are observed as in experimental poisoning. Terminal psychic disorders are characterized by stupor without the loss of the intellectual functions—they are only suspended. Add the loss of sociability, the panphobic tendency to isolate one's self, to conceal one's self, the frequency of sitophobia, or, on the other hand, hydromania, excitement exaggerated by attacks of systematized hallucinations.

Sitophobia explains itself in part by the presence of pyrosis and flatulent gastralgia, equally frequent in the experiments. Hydromania can be explained in several ways, for example, by burning sensations of the skin, by hallucinations, by the attraction of bright surfaces coincident at times with retinal changes and finally by blind impulses, comparable to those of epileptic automatism. In the course of these attacks of vertigo some of them may fall into the water, and their case is then regarded as one of suicide by drowning. All this explains, up to a certain point, the great number of deaths by drowning in Italy, in the districts where pellagra is prevalent. It may be admitted that the number of these deaths depends, up to a certain point, on the extension and the intensity of the pellagra. This extension is especially serious for Venetia and Lombardy since the cessation of the Austrian occupation, under which annual statistics were tabulated.

It is necessary to add to the nervous symptoms the frequency of spastic and tetanic phenomena.

The intermission of the symptoms is explained up to a certain point by meteorological influences which play an analogous role in alcoholism. The pellagrous are particularly sensitive to barometric changes.

Moreover it is important to note the very contradictory symptoms so often seen in pellagra: We note in fact frequently that there are:

Either	Or
Loss of appetite	Voracity
Somnolence	Insomnia
Sensation of burning	Sensation of cold
Mutism	Loquacity
Constipation	Diarrhea
Hydromania	Repugnance to water
Cataleptiform rigidity and immobility	Chorea and exaggerated mobility
Mydriasis	Myosis
Salaciousness	Impotence
Stupor	Mental excitement
Marasmus	Florid health
Apathy	Activity.

Here is reproduced in a double series of experiments with the poisons of corn a phenomenon already definitely established. The explanation is that there is a law common to almost all toxic substances, which is, in their action upon the animal organism they induce a series of opposite effects: a primary and a secondary action. It is thus that at

first aconite stimulates the cardiac plexus, the vessels of the heart contract, then the regular beating of the organ diminishes (slowness of pulsations, lowering of the temperature, etc.)—to these symptoms succeed others entirely opposite; the contrast is all the more visible when the stimulation of the myocardial nerves has been most energetic; the blood pressure increases, the heart beats more rapidly and the temperature rises. With small doses: daturin and hyoscin increase the arterial tension; with large doses the tension in the vessels diminishes, the intestines are paralyzed, the sensibility of the skin and the temperature diminish.

According to Brown-Sequard one can produce by small, progressive doses of ergot and of belladonna contraction of the vessels of the spinal cord and of the skin, and diminution of sensibility and the reflexes. Toxic doses, on the other hand, produced congestion of the meninges, convulsions and hyperesthesia. Poznanski has demonstrated that hydrocyanic acid taken in small doses can produce an acceleration of the circulation.

According to Regnaud opium taken in small quantities increases the activity and the circulation of the blood in the brain; in large doses it has the reverse effects. The same observation is noted in the stimulation of the motor functions and of cerebral activity by alcohol; these symptoms are followed by a profound depression of the circulation, of muscular force, of intelligence, and by a semi-stupor, etc. Such a variety of symptoms is discordant if observed from different points of view or in several indi-



viduals. Certain persons can undergo, by reason of peculiarities, the first or the second stages; and for this reason one ought to view aconite, alcohol, etc., sometimes as depressants, sometimes as stimulants, in accordance with the course of their action, according to the doses, the personal idiosyncracies and many other circumstances as well. But it is just this peculiarity of the symptoms of pellagra which proves that it is an analogous poisoning.

*Blood and Urine.*—The blood in pellagra certainly does not contain any trace of a special ferment or of any element of infection. Still, it more readily undergoes putrefactive changes. It is, however, not more deficient in fibrin than normal blood; except in the case of typhoid pellagra. This observation should disprove certain old theories about pellagra. The examination of the blood of non-cachectic pellagrins shows only a very small decrease of the red blood cells and not infrequently an actual increase.

[A moderate secondary anemia is quite constant in the experience of most observers and this has been our experience also. We have practically always found an appreciable reduction in hemoglobin.] There has been shown in typhoid pellagra in a few examinations a notable increase of urea in the blood. This fact taken in connection with a very frequent sclerotic nephritis and other morbid changes in the central nervous system and elsewhere allows the deduction that typhoid pellagra is an acute manifestation due to uremic or other complications. Hence Nardi, Verga, Rizzi and Strambio considered, with reason, typhoid pellagra as distinct from typhoid fever.

The complication of typhoid pellagra, if we may judge from our animal experiments, bears a close relation to the renal irritation produced by the poisons of corn; and the nephritis is probably of toxic origin. It is certain that all the phenomena of pellagra seem to indicate a preceding intoxication of the spinal cord and sympathetic system.

For the cardiac plexus this is shown in palpitations, hypertrophy and especially final atrophy of the heart, which, as we shall see, reaches a degree and a frequency such as is found in no other known malady. On this also depends edema of the articulations, scurvy and pulmonary emphysema. In the acute intoxication by the poison of corn, palpitations and syncope are produced as after the lesion of the sympathetic nerve; the systole becomes slower. More apparent still is the parallel between lesions of the sympathetic and disorders of the intestinal tract; these troubles show themselves suddenly in pellagra and disappear in the same way, being succeeded by entirely opposite symptoms: as anorexia and hunger, diarrhea and constipation.

Reflex uterine troubles, without apparent organic change on examination are frequently observed. The lesion of the sympathetic is much more evident in the numerous observed cases of inequality of the pupils, a common symptom in grave cases; and also in myosis and vascular dilatation on the same side which are the symptoms which C. Bernard, Biffi, and others have described as following section of the sympathetic. In these cases there exists a corresponding hemicrania. Is it not probable that in other cases,



as it is certain in this, the cause of the headache and perhaps of the vertigo and of the hyperesthesia may be entirely ganglionic and depend upon a hyperemia produced by ganglionic paralysis?

It is to be noted in this connection that the various painful reflexes and the cerebro-cardiac neurosis, palpitations, trismus, etc., can be made to disappear by electric stimulation of the cervical ganglion. Going a step further could we not with time relegate to this cause even the cutaneous lesions of pellagra, whose dependence upon the nervous system is indicated by such associated symptoms as pruritus, sensations of heat and hyperesthesia? The frequent pyalism of the pellagrous is also physiologically connected with the disorders of the sympathetic. The experimental spinal symptoms, the numerous cases of spastic paralysis, tetanus, the increase of the reflexes and of the muscular tonus, the tremor, the motor incoordination of the superior extremities denote, as Belmondo says, the degenerations of the crossed pyramidal tracts and of the gray matter of the spinal cord, as pathological anatomy makes it appear; likewise hyperesthesia and delirium denote a cerebro-spinal meningitis.

*Weight.*—The loss of body weight is not always (as has been seen) a constant symptom of pellagra (Strambio). It is found, however, in 84% of the cases of women and 74% of the men. Calderini finds out of 1,005 cases 514 notably under weight. In general the diminution of the weight proceeds parallel with the progressive repugnance to food. It is a clinical symptom of prime importance, as it is also

in experimental animals. The average weight of 108 pellagrous women was 44.6 kilograms, that of 100 pellagrous men was 62.5 kilogrammes. However, there were found among the women 6 who went beyond 58 kgr. and one of 68 kgr.; among the men 12 weighed more than 50 kgr., 6 more than 54 kgr. and 8 more than 60 kgr. One man, who died of acute pellagra, weighed 86 kgr. and had a strong muscularity. Another man, very old, with a form showing a tendency to vertigo, weighed 72 kgr.

Calderini finds in 1,005 cases of pellagra 491 with full and florid faces; according to Nardi and Nobili the cases showing an evident diminution of weight seem more curable than those which show an increase. The half, at least, of the most severe cases of typhoid pellagra are observed in individuals well nourished and of strong constitution. This is explainable when it is a question of young persons, or, indeed, of the well-to-do classes. Cases of this kind have been observed by Odoardi, Alpago-Novello, and it is known, indeed, that persons in good circumstances are not only heavier, but taller than poor people.

**THE SKIN:** The skin presents, besides the customary general phenomena of erythema and telangiectatic spots, not infrequently other peculiar appearances. Landouzy and Lombroso have noted not rarely a pigmentation of a chocolate or bronze color, and a thickening of the epidermis in sites of a previous erythema. Certain pellagrins affirm that at the beginning of the disease the skin of the entire body has assumed a darker hue. In many of the sick are found ephelides and chloas-

mata scattered principally over the brow and chest. Sometimes each spring the chloasmata were preceded by red spots on the face which resembled the eruption of rubeola. In the case of an old female pellagrin, who suffered from brachial neuralgia, the entire skin was of a bronze-like color and the arms showed an eczema of a scaly nature which later became ulcerous.

Premature and extensive wrinkling of the skin has been observed, and increased activity of the sweat glands even in winter. The phenomenon of a species of antagonism between the appearance of cutaneous symptoms and the nervous and muscular disturbances of pellagra, once observed in animals, was also seen three times in about one thousand cases. One case in which there had been for two years vertigo, burning sensation on the back, diarrhea and melancholia, enjoyed entire relief from these symptoms upon the appearance of a persistent acne rosacea; in another case an old man of eighty-two years showed improvement in his pellagrous manifestations after the appearance of a scaly herpes upon his face; in a third case a woman of Novaro, thirty-four years old, with pellagrous delirium and a marked cachexia, having developed smallpox regained her calm and was even relieved of a pellagrous diarrhea.

Others have likewise observed that the desquamative lesions of the skin bear no relation to the gravity of the disease. Strambio says: "And, indeed, although often in the beginning their unsightly scaly eruption is sufficient to excite the pity of all,

still, after a few days all the skin manifestations will disappear. Therefore, the intensity of the disease is not to be measured by the scaly eruptions." [It has been our experience that extensive, moist dermatitis is almost always associated with grave constitutional disturbances. Similar reports are made by other American observers.]

A rare symptom in the neighborhood of Pavia—while in Venetia and Tuscany it is frequent—is the dilatation of the venules of the face, especially of the nose, which gives the pellagrin the appearance of a toper. Very often a brownish color of the skin is observed, particularly of the face, especially in the country districts of the southern Tyrol.

In only three cases was there found edema of the eyelids and traces of edema of the feet. In four cases thickening of the finger nails was noted, twice on the right side only.

**HEAD AND ORGANS OF SPECIAL SENSE:** Anomalies of the cranium are rare among pellagrins even when insane. They are more frequently found in other insanities—about eight per cent. in the former and over twenty-one per cent. in the latter. The only exception to this rule is found in hereditary pellagrins, a great part of whom show a general increase in cranial diameters with a relative predominance of the transverse diameter, similar to what is seen in cretins. In these hereditary pellagrins are also found numerous deformities of the skeleton of the face (eurygnathism and prognathism) which remind one of the negroid and mongolian types of degeneracy. Diverse peripheral anomalies are likewise very numerous among hereditary pellagrins.

**EYE SYMPTOMS:** Remarkable peculiarities are found in the eyes of the pellagrous; a falling of the supercilliary fold is very frequent in severe cases—even unilateral ptosis is not rare. Inequalities of the pupils are very important and dilatation in the right eye is very frequent. In many cases is found also a marked unilateral injection of the conjunctiva. These are observations which remind one of general paresis, and show, along with other manifestations, how frequently the lesions of the nervous system may be unilateral, especially lesions of the sympathetic system.

Very often also (74 cases) mydriasis of the two sides is found. Myosis is more rare and when found is more usual in the aged. Cases of blepharitis are not rare as was shown by the Piedmont commission. Often also diplopia, photophobia and synchysis are found. Many pellagrins remain for years with their eyes closed for fear of the light. Early cataracts are found among the pellagrous; and pterygium is not infrequent. Dr. Ottolenghi, with Professor Manfredi and Dr. Flarer have made ophthalmic studies on pellagrins. Their results are given in the following table:

Number examined.. . . . .	36
Depth of eye normal.. . . . .	12
Changes in the retina.. . . . .	15
Atrophy of arteries.. . . . .	12
Anomalies in fundus of left eye.. . . . .	1
Anomalies in fundus of right eye.. . . . .	6
Atrophy of optic nerve.. . . . .	3
Increase of pigment.. . . . .	3
Dilatation of the veins.. . . . .	1

Fifteen of these cases showed retinal changes by a yellow or gray reflex in one or both eyes—a sign of precocious senility; it is of interest to note that there were three cases of white atrophy of the papillae, among which was one case of retino-choroiditis in an advanced stage. Ottolenghi found also in three pellagrins one light case of papillitis, more pronounced in the left eye; in the second case pronounced gray atrophy and diffuse retino-choroiditis of the two sides; the third was normal. It is of interest to note the observation that in several individuals the ocular fundus differed on the two sides. This, however, cannot be given as a reason for the numerous pupillary inequalities since these are noted in individuals who show a normal fundus. However, the unilateral anomalies of the fundus as well as those of the pupils predominate in the right eye and consist in lesions of the arterial vessels with papillary and retinal changes. Rampoldi observed pellagrous ocular troubles principally in the autumn or the spring, and found that they consisted of organic lesions rather than functional disorders. The retina and optic nerve show more than any other part of the eye the pellagrous cachexia, next come the cornea and lens; finally the choroid and vitreous body. Hemeralopia and pigmentary retinitis are not rare. Torpid ulcers of the cornea are found with essential hypotonus of the bulb and scintillating synchysis of the vitreous.

[We are indebted to Dr. E. M. Whaley, of Columbia, S. C., for the following report on



**"EYE FINDINGS IN THIRTY-FIVE PELLAGRINS.**

"The number of cases examined was thirty-five, their ages varying from eight to seventy-six years, only two of whom showed normal eyes.

"The appearance of the patients was that they did not carry their upper lids as high as they should, thereby giving the appearance of general lassitude. In considering this report it should be remembered that more than half of the patients we are dealing with are afflicted with insanity, which would naturally make us expect to find the nervous element much in prominence and the disease well advanced, except a few in whom it has developed since their stay in the hospital and among the younger subjects.

"All pellagrins are unresponsive and no field examination could be made; with few exceptions the examination had to be made while the patient was in bed. The dilated pupil so much spoken of by the Italian observers was not so prevalent with us, it having occurred bilaterally in three cases only; unilaterally, in two cases, and one of the bilateral cases was myopic. Two cases resisted the action of homatropine for two hours, four resisted it less strenuously, while the others reacted in the usual twenty minutes. Hypersensitiveness to light with contracted pupils was the rule.

"Shallow anterior chambers were found in thirty-three per cent. of the cases. Strabismus could not be detected when there was not other evident cause. Where the gastro-intestinal symptoms are very pronounced and the inflammation extends to the mouth and post-nasal space, we find an obstruction of the lachrymal duct due to continuity of surface.

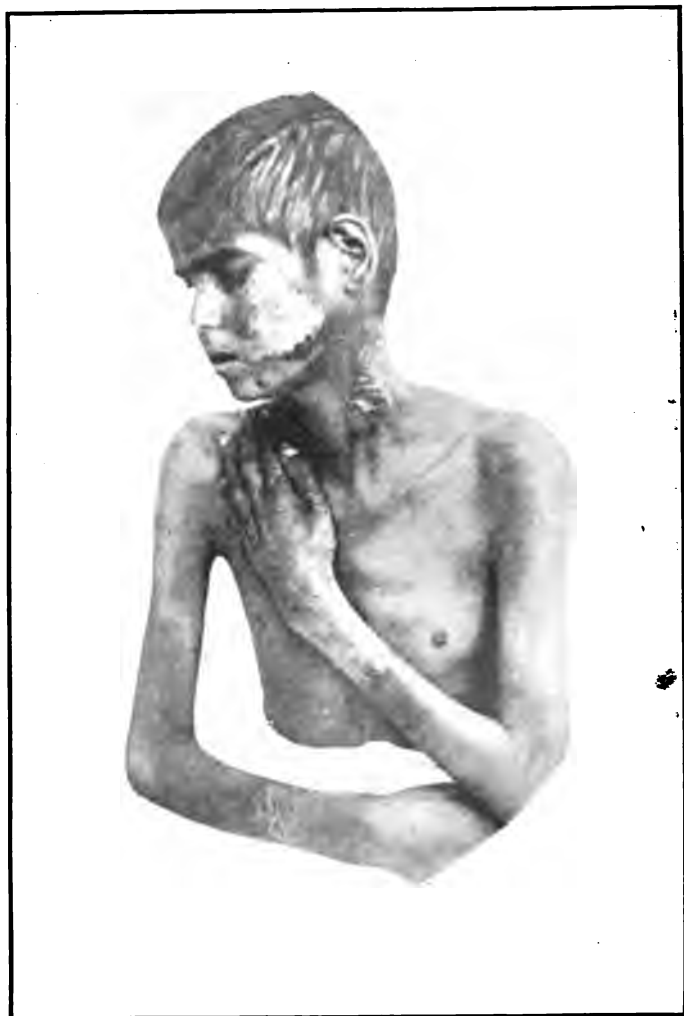


Plate XII. Egyptian case. Compare with Plate XI. Courtesy of Dr. F. M. Sandwith.





This was noted in five cases all of which had the mucous membranes very much affected by disease. Photophobia of slight degree without the inflammatory changes which usually accompany this condition was present in six cases.

"The findings as tabulated are as follows:

*"Lids:* Paretic, one; lachrymation, two; dachryostitis, two; conjunctivitis, two; muddy conjunctivae, two; jaundiced conjunctivae, three; obstruction of lachrymal duct, five.

*"Corneal Abnormalities:* Ulcer, four; superficial inflammation, two; increased sensibility, two; subnormal sensibility, seven.

*"Muscles:* Paresis (right rectus), one; nystagmus, one.

*"Anterior Chamber:* Shallow, twelve; deep, one.

*"Iris:* Iritis serous, one; sluggish reaction to light, six; hypersensitive, four; photophobia, six; reaction to homatropine, slow, four; prompt, one; spastic reaction to light, two.

*"Pupils:* Unilaterally dilated, two; bilaterally contracted, three; bilaterally dilated, three; Argyle Robertson, one.

*"Tension:* Plus bilateral, one; plus unilateral (O.S.), two.

*"Fundus:* Retinitis, two; detached retina, one; optic atrophy, three; optic neuritis, three.

*"Lens:* Cataract bilateral, three; unilateral, two; cloudy lens, one.

*"Arteriosclerosis,* fifteen.

"After examining somewhat over half of these cases, I found that there was most common a dilatation of the retinal veins and a somewhat yellowish

reflex from the retina which I do not recall having seen elsewhere. This appearance is hard to describe, appearing as a thickening of the retina itself.

"The arteriosclerosis which appears in so many of the cases is of every stage and occurs in the young as well as in the older cases.]

*Thoracic and Abdominal Organs:* Strambio noted the slow pulse rate in pellagrins, a decrease often to 40 and even to 34 per minute. Lombroso, however, has more often noticed a rapid pulse, 100 to 105, frequently filiform in character and difficult to feel. In three-fourths of the cases, principally in the young, a sensible diminution is found in cardiac force. The apex beat is often not visible, sometimes barely perceptible on palpation, and is frequently displaced downward and outward between the sixth and seventh ribs, to the breadth of two to four fingers and a half below the nipple. Frequently the sounds of the heart are difficult to hear. In aged persons, however, the left ventricle is often hypertrophied, there is mitral insufficiency with dilatation, and the first sound at the apex is replaced by a blowing murmur.

*Gastric Symptoms:* Pyrosis and eructations are very frequent. Constipation is observed usually in those upon whom the disease has not produced profound effects. Sitophobia is a frequent condition in insane pellagrins, but even the non-insane cases often show profound repugnance for food, especially meat, and, strange to say, polenta; on the other hand, many suffer from a continual bulimia and will consume a quantity of nourishment double or triple that of a well man. A pellagrous woman exhibiting

this voracious appetite, a little before delirium set in, left her house in order to keep from devouring her children.

With regard to liquids also the pellagrous often show marked peculiarities. Many complain of an unquenchable thirst and drink enormous quantities of water. Others have a great repugnance for liquids. One complained that after having drunk she had the sensation of a stone in her intestines. Many find a salty taste in water; others have a repugnance for cold water and must drink the water hot or lukewarm.

Lombroso, Filippi and Roncoroni examined the gastric juice of two pellagrins. The stomach was found almost completely empty, the first time four hours after food and the second time one and a half to two hours thereafter. The test meal consisted of a porringer of soup, 85 grams of meat, 200 grams of bread and 100 grams of wine. Four tests were made on each individual. Hydrochloric acid was found to be generally diminished and the presence of lactic acid frequent. The following table gives full results:

Analyses.	Case 1.	Case 2.
Reaction of gastric juice.	Once neutral; three times slightly acid.	Acid.
Hydrochloric acid (Gunsberg reaction).	Always negative.	Always negative.
Lactic acid (Uffelmann reaction).	Present three times out of four.	Always appreciable.
Percentage of acidity.	Average, 60%.	Average, 50%.
Peptone (Biuret reaction).	Present.	Present.
Digestion of starches	Twice complete; once arrested in the second stage.	Three times complete; once arrested in the first stage.

[Nesbit at the National Conference on Pellagra, 1909, reported the results of the analyses of the stomach contents of 10 cases of pellagra. Four showed a marked diminution in the acid factors of the gastric juice in the late stage of the disease. Five showed an excess of mucus during the pellagrous periods. Six showed normal motility, while in three the motility test was not made. Four showed the presence of bile during severe vomiting periods. He remarks that while this series of cases is too small for definite conclusions, the indications are that in pellagra, as in all adynamic and asthenic diseases, the hydrochloric acid and ferments of the gastric juice are progressively diminished.]

The *Genito-Urinary* functions present phenomena worthy of note. Even though the urine be clear many of the pellagrous complain of a burning pain on urination; others feel a sensation of heaviness and of cold in the groin or around the uterus; others complain of a retraction of the penis, or again a sensation of painful heaviness in the testicles. In many of the hereditary pellagrins the hair around the genitals is wanting and the testicles are atrophied. In hereditary pellagrous women are noticed atrophy of the breasts, irregularity or absence of the catamenia, which is sometimes followed by a painful metrorrhagia.

Calderini notes dysuria in 74 per cent. of the men, and in 57 per cent. of the women, amenorrhea in 50 per cent, leucorrhea in 50 per cent. and abortion in 17 per cent. Many cases suffer from subjective sensations of uterine inflammations or displacements

without objective signs. A robust country woman in the hospital at Verona, thirty-one years old, the mother of five children, complained of violent pain on urination and a sensation of weight in the uterus, "as if it were made of lead," with burning at the cervix uteri. She would not tolerate a speculum for examination, but was treated a long while for metritis. Finally she began to complain of epigastric swelling, burning on the back, alternate sensations of hot and cold, and had diplopia; later she developed a melancholic mutism without adequate cause. It was then thought that perhaps the uterine symptoms might be of a pellagrous nature. A careful examination with the speculum showed no trace of a metritis. It was a case of unrecognized pellagra.

[At the National Conference on Pellagra, 1909, Eleanor B. Saunders presented a very thoughtful paper on the gynecologic, obstetric and surgical aspects of pellagra which is well worthy of serious attention in this connection. Surgeons, especially gynecologists, should bear pellagra in mind if they would avoid occasionally useless, and even harmful procedures.

Dr. Saunders's paper is summarized as follows:

"To sum up my observations and reading upon the aspects of pellagra embraced in this paper, of the 24 cases reported, 4 patients are still under treatment, 10 recovered, and 10 died. In America and Roumania the female sex is more liable to pellagra, the periods of greatest incidence being the twentieth to fortieth year. *Obstetric*.—Pregnant women suffering from pellagra are liable to abortion (17 per cent.), to give birth to still-born infants, and at delivery to post-partum hemorrhage. Gestation and lactation, especially



when frequent, predispose to pellagra. Parturition is often an exciting cause for the outbreak of the dermatitis. *Gynecologic*: amenorrhea and leucorrhea occur in 50% of the cases, and dysuria in 57%. Unmarried female pellagrins are more subject to amenorrhea. Multiparous pellagrins are liable to menorrhagia, and present symptoms suggesting cancer. Their subjective symptoms may point to diseases of the pelvic organs and require careful examination for their exclusion. Not uncommon are vulvitis, vulvovaginitis, cervical erosions, endocervicitis and endometritis, ovarian neuralgia and inflammation, maceration and denudation of adjacent skin on the thighs and in perineal and anal regions, especially in 'moist' cases. A *surgical* operation may bring out latent pellagra. Diseases of the kidney are simulated and may be primary or secondary. Stomach symptoms are often so severe as to require attention and rigid diagnostic methods. Care should be exercised to prevent needless surgical or other treatment. Other subjective symptoms may annoy the patient to such an extent as to demand treatment. Pellagrins often complain of symptoms suggestive of hemorrhoids when it is really proctitis, a part of the general inflammation of the intestinal mucosa and adjoining epidermis. In essence, pellagra may be a trophoneurosis, but that in women the pelvic organs are especially subject to the invasion of the unknown poison, is a fact demanding wider recognition as well as further study.

"In asylum life we see a few failures among many brilliant surgical successes, but the above surely points to the fact that in the initial stages, especially when the symptoms are not very well marked and when there is much pointing to pellagra as well as to other diseases, a very careful differential diagnosis should be made and care given to other than the pelvic symptoms of these cases. If possible, relieve the primary disorder, pellagra, before resorting to radical operations, which, at best, cannot cure pellagra, and will probably only increase the already lethal tendency. Not much will be lost in waiting for a time, at the expiration of which the symptoms may have been relieved, or the pellagra

erythema now so necessary for diagnosis have appeared in full efflorescence. Patients with pellagra, on account of their debilitated condition, are prone to other diseases, and are subject to 'Incidentals' which require surgical intervention. These demand and should have prompt attention, but after granting all this, I am forced to believe that the majority of such patients should be treated not as having a primary organic pelvic disease, but as suffering from functional or symptomatic disorders, and, furthermore, that the gynecologic, obstetric and surgical aspects of pellagra are factors which not only the general practitioner must consider, but with which specialists of several kinds who live in the pellagra zone must hereafter reckon for the real welfare of their patients."]

**THE BLOOD:** In a study of eighteen cases of pellagra it was made apparent that there was no decrease in the number of red cells or in the quantity of fibrin as had formerly been the opinion.

TABLE OF THE QUANTITY OF FIBRIN AND NUMBER OF RED CELLS IN EIGHTEEN PELLAGRINS.

Number.	Age.	Sex.	Quantity of Dried Fibrin by Weight.	Cell Measurements.	Number of Red Cells.	Remarks.
1	40	Male.	0.157%	4	5,125,000	Robust.
2	21	Male.	0.169%	..	.....	Thin.
3	50	Male.	0.400%	3	5,250,000	Very robust.
4	49	Male.	0.260%	3	5,250,000	Emaciated.
5	46	Male.	0.008%	..	.....	Emaciated.
6	19	Male.	0.201%	..	5,000,000	Fat.
7	56	Male.	0.150%	5	.....	Very robust.
8	18	Male.	0.173%	..	4,875,000	Robust.
9	25	Female.	.....	6	4,625,000	Very robust.
10	41	Female.	0.180%	8	.....	Typhoid pellagra.
11	37	Female.	0.350%	8	4,250,000	Emaciated.
12	40	Female.	.....	11	4,500,000	Convalescent.
13	38	Female.	0.009%	9	5,125,000	Typhoid pellagra.
14	38	Female.	0.282%	4	4,625,000	Convalescent from typhoid pellagra.
15	45	Female.	0.013%	8	5,125,000	Typhoid pellagra.
16	45	Female.	0.173%	4	5,250,000	Convalescent from typhoid pellagra.
17	43	Female.	0.024%	3	5,250,000	Robust.
18	29	Female.	0.157%	3	5,250,000	Robust.



From an analysis of this table it is seen that ordinarily not only is the fibrin not diminished, but sometimes it is even increased (2 cases in 18); in four cases in which it was diminished, two were typhoid pellagra, and in these after the disappearance of the typhoid symptoms the proportion of fibrin again became normal. The diminution of fibrin, therefore, cannot be regarded as a sign of pellagra. The number of red cells appears almost constantly to follow the fibrin, no sensible diminution was noticed except once in a woman convalescent from pellagra who was subject to malaria and lived in a fever district (Certosa). The diminution of the number of red cells is not sufficient to justify one in talking of anemia; it was noted, however, in three cases of typhoid pellagra. These results are confirmed to a certain degree by studies made with the Bizzozero instrument by Sepilli at the asylum for the insane at Reggio. He found in 55 pellagrins

13 (23 per cent.) showing 80-95 per cent. hemoglobin.

15 (27 per cent.) showing 60-85 per cent. hemoglobin.

18 (32 per cent.) showing 50-65 per cent. hemoglobin.

4 ( 7 per cent.) showing 30-50 per cent. hemoglobin.

[Five of these cases are omitted.] From these results it is obvious that a fair number of pellagrins do not suffer any reduction in hemoglobin; and consequently anemia, while a frequent, is not a constant characteristic of pellagra. This accords with the experimental work done on dogs.

These observations serve to show the uselessness of treatment with iron, a remedy which has been much employed; the ferruginous district of Ricoaro con-

tains a large number of pellagrins. Several authors, as Liberali and Robolotti, have even recommended the letting of blood. The drawing of 100 to 150 c. c. of blood practiced in the course of hematological researches on pellagrins, even in typhoid pellagra, appeared harmless, though sometimes beneficial.

The examination of the blood of an hereditary pellagrin of Régis, made by Professor Sabrazès, gave this result:

Hemoglobin.. . . .	.75 per cent
Coagulation time (Sabrazès method) . . .	9 minutes, 12 seconds
Red cells.. . . .	2,449,000
White cells.. . . .	6,200

On bibulous paper the blood made a clear spot without a watery border; no red cells with basophilic degeneration; inequalities in the size of the red cells with numerous microcytes; some poikilocytes; a few polychromatic red cells; no nucleated reds.

Polynuclears.. . . .	63.3 per cent.
Lymphocytes.. . . .	32.6 per cent.
Mononuclears.. . . .	3.4 per cent.
Eosinophiles.. . . .	.7 per cent.

Lumbar puncture was also done. The examination of the cerebro-spinal fluid was negative.

[The next table shows results obtained by us in blood counts made at Columbia, South Carolina:



Number.	Sex.	Color.	Age.	Per Cent. Hemoglobin (Dare.)	Number White Cells.	Number Red Cells.	Mental Involvement.	Arsenic.	Remarks.
1	male	white	60	75	4,000	3,424,000	no	no	Chronic, mild, neurasthenic.
2	male	white	60	75	8,600	4,634,000	no	yes	Chronic, mild, neurasthenic.
3	male	white	60	64	6,222	4,272,000	no	yes	Chronic, mild, neurasthenic.
4	female	colored	52	65	4,508	4,842,000	yes	no	Chronic, mild.
5	female	colored	52	83	10,115	4,824,000	yes	yes	Chronic, mild.
6	female	colored	25	45	6,755	4,868,000	yes	yes	Emaciated, wet erythema, spasticity.
7	female	colored	30	45	4,800	4,888,000	yes	yes	Emaciated, dry erythema; paralytic.*
8	female	colored	25	45	8,266	2,826,640	yes	yes	Emaciating; wet erythema; improved.
9	female	colored	35	38	9,633	2,920,000	yes	yes	Fairly well nourished; dry erythema.
10	female	colored	25	64	13,000	4,148,800	yes	yes	Emaciating; wet erythema; increased reflexed.
11	male	white	39	88	7,066	5,520,000	no	no	Dry erythema; neurasthenic; alcoholic.
12	female	colored	25	38	6,044	3,400,000	yes	yes	Slight emaciation; dry erythema; syphilis; round worms.
13	male	colored	38	95	8,200	5,500,000	yes	yes	Well nourished; much excited; dry erythema.
14	male	white	55	57	11,980	3,800,000	yes	yes	Arterio-sclerosis; dry erythema.
15	female	colored	16	88	13,066	4,686,000	yes	yes	Generalized, wet erythema; emaciating paretic.
16	female	white	31	59	10,844	5,604,800	yes	no	Well nourished; dry erythema; paretic.
17	female	colored	22	74	9,754	3,864,000	yes	no	Well nourished; dry erythema; hookworms.
18	female	colored	44	70	17,310	4,708,000	yes	no	Dry erythema; arterio-sclerosis; much excited.
19	female	colored	37	76	5,544	5,008,000	yes	no	Pellagroid; diagnosis doubtful.
20	female	colored	33	96	8,880	4,620,000	yes	no	Cured case; no symptoms for over a year.
21	female	colored	50	93	7,344	4,440,000	yes	no	Cured case; no symptoms for over a year.
22	female	white	25	80	17,400	4,976,000	yes	no	Suicidal and excited; dry erythema; losing weight.
23	female	colored	38	86	12,010	5,504,000	yes	no	Dry erythema; slight loss of weight; mildly excited.
24	female	white	22	60	5,800	4,580,000	no	no	Chronic, mild.

\*The word paralytic in this table is used in the sense adopted by writers on pellagra, that is paretic rather than actually paralytic.

The technique of making these counts was as follows: The Thoma-Zeiss counting chamber, with Turck's ruling, was used; in counting red cells the four corner unit squares (25 small squares each) were counted in two preparations, and if the results were discordant a third was counted; in counting white cells the whole ruled space was counted in two preparations; and again, if results were discordant, a third preparation was counted. The hemaglobin estimation was made with a new Dare instrument, which gave very uniform readings in normal individuals.

The cases were mostly of an advanced type with many secondary nervous changes, and nearly all alienated. Most of them were negro women. The greatest number of the counts were made at the same time of day (morning) and under the same circumstances as far as possible. Many of the patients had been taking arsenic in some form with full doses, either at the time of the examination or not a very long while previously.

A brief analysis of this table shows a frequent reduction in red cells and in hemoglobin and the color loss would seem proportionately greater than the cell loss (chlorotic type of anemia.) There is a great variation in the number of leucocytes, with an occasional decided leucocytosis not clinically explicable by complications or otherwise. It is interesting to note that numbers 1, 2 and 3 in the table are the same individual, before and after arsenical treatment; and likewise 4 and 5 are made in the same individual; 19, 20 and 21 are also of interest as doubtful or cured cases.

Differential leucocyte counts were made in several of these cases. The results generally showed a relative, large mononuclear increase with an absence of eosinophilia, except in cases with such complications as round worms or hookworms. We do not tabulate these counts, as we do not find the work satisfactory and distrust the results. The general literature of pellagra is somewhat discordant as to results obtained in differential, leucocyte counts. A majority of workers report, however, a relative, large, mononuclear increase, with an absence of eosinophilia.

With regard to qualitative changes in the red cells, we found the ordinary changes of a secondary anemia, the degree of such changes depending, of course, on the grade of the anemia.

In bacteriological work on the blood, both by culture and with animals, our work has been uniformly negative. We have followed Tizzoni's technique repeatedly in the attempt to isolate his *streptobacillus pellagrae*, but have met with no success.

From a review of the literature, and from our own work, it would seem to us that secondary anaemia is a frequent, though not constant, condition in pellagra; that leucocytosis is not often seen and is probably not a phenomenon of the uncomplicated disease; that conclusions from differential, leucocyte counts, at present, are uncertain, but that there is probably a relative, large, mononuclear increase; that no protozoal parasite has yet been found in the blood; and that both by ordinary culture methods and with animals the blood is found sterile.]

**THERMIC PHENOMENA:** Bonfigli, who regards pellagra as due to inanition, has found fever in 20 per cent. of his cases. The temperature is oftenest found normal except in the tetanic or so-called florid forms.

Alpago-Novello, at the hospital of Feltre, studied 100 cases in which he took axillary temperatures morning and evening, leaving the thermometer fifteen minutes alternately on the right and on the left sides. Of the 100 pellagrins there were 63 men and 37 women; two were less than 20 years old; 39 were from 20 to 50 years old; and 59 were above that. Six were in the first period of disease, 35 in the second and 59 in the third. Control observations were made in ten hospital patients suffering from non-febrile maladies. Among the ten control cases 1,607 observations were made. They showed a minimum of 35° C. and a maximum of 38.5° C., and this occurred once only, being probably caused by constipation, and disappearing promptly after purgation. The average temperatures in the ten controls were: in those above normal 37.38; in those normal 36.58; and that of the entire series 36.60, which, as will appear, is .35 of a degree less than the same average in pellagrins.

Altogether on the 100 pellagrins 22,274 individual observations were made, which oscillated between a maximum of 41.5 degrees and a minimum of 35 degrees. Above the normal temperature there were 2,059, below the normal there were 5,251. Thus, then, the former made 9.24 per cent. and the latter 23.57 per cent. of those that varied from the normal.

Of the temperatures above the normal, 2.11 per cent. were taken in the morning (471) and 7.13 per cent. in the evening (1,588). In twelve pellagrins only out of the 100 was there no abnormal increase of temperature (one in the first period, ten in the second, and one in the third). The average temperature in all the cases was 36.95 degrees; the average of the febrile temperatures was 37.96 degrees, only one degree higher than that of the average of the total observations.

It may be concluded, then, that the average temperature is higher in pellagrins than in the control cases. In 88 per cent. of the cases it reached a febrile state and in some a high degree of fever. The elevation of temperature takes place rather in the evening than in the morning.

The condition of the pellagrous patients according to their temperature and the period of their disease furnishes the following facts:

In six cases of the first period, temperatures above the normal were found only 17 times, or 3.82 per cent. The maximum was 39 degrees, but it showed itself only one time and did not return. In another case the elevation did not go over 38 degrees. In all the other cases it remained below this figure. The average of all the experiments in this period of the disease was 36.72 degrees. In one case only, consequently 16 per cent., was there no febrile temperature.

In the 35 cases of the second period, there were 6.01 per cent. above the normal, or twice as many as in the cases of the first period. In one case the

temperature rose to 39.4 degrees, in another to 39 degrees; in 14 cases it oscillated between 38 and 38.9 degrees; in 19 cases it was below 38 degrees. The average of all was 36.81 degrees, or 0.09 of a degree higher than the average of the cases of the first period. There were ten cases without a trace of febrile temperature, that is 28.57 per cent.

The tendency to a febrile state is more accentuated in the third stage. Of these there were 59, and the temperature was found above normal 1,745 times, which is 10.12 per cent. of the total observations, being nearly double that of the second stage. The highest temperature observed was 41.5 degrees; the others were as follows: 40 degrees and above in 11 cases; 39-40 degrees in 23 cases; 38-39 degrees in 17 cases; below 38 degrees in 8 cases. The average of all the observations was 37.06 degrees; it was, therefore, more elevated by a quarter of a degree than the average of the cases of the second stage. A single case, that is 1.7 per cent., showed no fever, but still it ought to be stated that this case reached the maximum of the normal temperature, that is 37.4 degrees.

An observation which may have a certain prognostic interest, is that the twelve patients whose temperatures had not been above normal during their stay at the hospital, left it cured with one exception, and this one case showed no improvement. Analogous results are obtained by observing the cases at different stages.

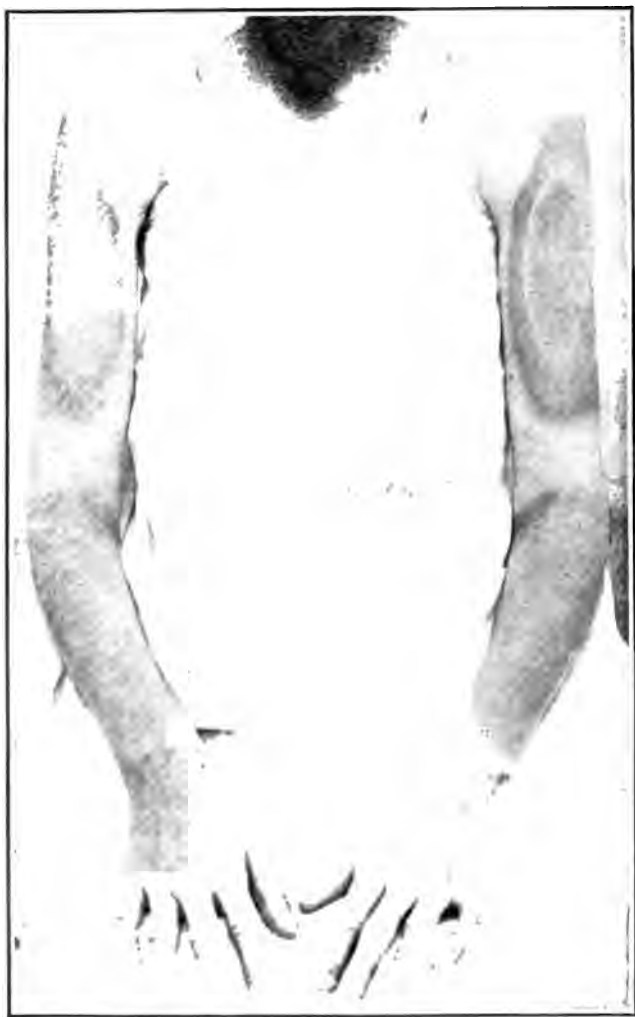
The temperature increases during the passage from the first to the second or from the second to the



third stages. For example, in one case the highest temperature in the first stage was 37.5 degrees with an average of 36.98 degrees; in the second stage the highest was 38.1 with an average of 37.14 degrees. So, in another case, the second stage was afebrile, with an average of 36.60 degrees, while in the third stage there was a maximum of 40 and an average of 36.82 degrees. But even in the course of a single stage in a febrile case, Alpago-Novello was able to assure himself that the improvement of the patient proceeded *pari passu* with a gradual decline of the temperature. And he was able to state that *vice versa*, the aggravation of the disease proceeded step by step with the rise of the temperature. This accords with the experiments on dogs in which the aggravation of the symptoms of intoxication occurred at the same time with the maximum of temperature and minimum of weight.

Of the 38 pellagrins who died of the disease, 28 had in their last days a febrile temperature; nine did not. Likewise with dogs, temperature elevation runs parallel with diminution in weight, and increases at the approach of death.

The course of pellagrous fever is absolutely irregular. It is rarely continuous, is often remittent, almost always with an evening rise; it is frequently intermittent (the rise usually occurring in the evening), and there is always a great irregularity both in course and in elevation. Often there is a fever disturbance at varying intervals. In the cases of typhoid pellagra Lombroso and Belmondo have noted some rare conditions of subnormal temperature (33 degrees) in the last days of the malady.



**Plate XIII.** Illinois case. Pellagrous "gauntlet" and unusual localization on arms. Courtesy of Dr. G. A. Zeller.



Roncoroni and Lombroso followed attentively three patients for five days and the difference in the sides was almost regularly .1 to .2 of a degree, and in two cases especially a higher temperature was noted on the left axilla. In another series of observations of 12 pellagra patients the temperatures on the left; twice only it was equal. [See charts.]

URINE: Of 100 pellagra patients the quantity of urine in twenty-four hours showed an average of 900 c. c., with a minimum of 500 c. c. and a maximum of 1,900 c. c. The quantity is, therefore, less than normal. Calderini also found in 35 per cent. of his pellagra patients a great diminution of the quantity of urine. The reactions of the urines of pellagra patients show a marked difference from the normal. In 100 cases the urine was: 76 times slightly acid; 14 times neutral; 10 times alkaline. It is in the most severe cases that the urine is more often alkaline (paralytics and aged patients); but also in young patients having cataleptiform or epileptiform attacks Calderini has made the same observation. Also in an examination of 33 cases, he found 21 per cent. of the urines strongly acid, 57 per cent. of slight acidity, 12 per cent. neutral, and 9 per cent. alkaline. Verga found 11 per cent. of the urines alkaline and 21 per cent. neutral. The color of the urines is constantly pale yellow, never passing the numbers 3 and 4 of the Vogel scale. The specific gravity is always less than the normal; it varies between 1,005 and 1,010, and between 1,018 and 1,025.

A remarkable peculiarity of the secretion of urine is its constancy; even at the approach of death pellagra patients show very little change in the quantity, color and reaction of the urine. And in pellagrous meningitis and typhoid pellagra one finds, with a pulse of 120 and a temperature of 39 to 41 degrees, the specific gravity of the urine is often less than normal. Roncoroni has examined the constituents of the urine in three cases, particularly with regard to the urea (by Esbach's method), the phosphates and the chlorides. As a means of control the urine of three epileptics, while free from attacks, was taken. The persons under observation were placed under the same regimen. They were put on a daily diet equivalent to 147.41 grams of albumen and casein, 567.27 grams of fats and carbohydrates, 22.891 grams of proteids, and 48.913 grams of urea. The observations were continued for ten days. The average results were:

	Pellagrins.	Epileptics.
Weight in kilograms.....	52.43	60.10
Urine in cubic centimeters.....	1,185.00	1,303.00
Specific gravity .....	1,014.50	1,018.07
Total urea .....	21.74	28.40
Urea per kilogram of body weight.....	0.41	0.43
Total phosphates .....	0.985	1.692
Phosphates per kilogram of body weight.....	0.018	0.027
Total chlorides .....	10.16	11.43
Chlorides per kilogram of body weight.....	0.20	0.185

In pellagrins the total amounts of urine and the specific gravity were diminished. The quantity of

urea was appreciably less than the normal in both epileptics and pellagrins, but in the latter this was more pronounced. On the other hand, in relation to the body weight, the urea was notably greater in the epileptics.

We can say almost as much of the chlorides; the total quantity of these is likewise less, but estimated per kilogram of the body weight it is a little higher in the pellagrous than in the epileptics.

A notable difference is to be found in the quantity of the phosphates. While the epileptics, during the time that they are free from attacks, eliminate an average of 1.692 grams of phosphates in twenty-four hours, or 0.027 gram per kilogram of their weight, the pellagrous, on the other hand, eliminate only 0.985 gram or 0.018 gram per kilogram of body weight, that is, less than half the quantity of the phosphates eliminated normally, which is estimated at 2 to 3 grams in twenty-four hours.

The difference is very perceptible between the percentages of urea and of phosphates eliminated in the urine of pellagrins and in that of epileptics, which is respectively 4.36 and 6.45.

Notwithstanding the rich diet which was given to the pellagrous patients under observation, the changes in nutrition were marked.

Out of 110 urines of pellagrous patients albumen was found only twice by use of the usual reagents, six times by heat and nitric acid no trace of albumen was found, but cylinders were revealed by the microscope. In one case they appeared for several days and then disappeared completely. In general,

albuminuria is rare in pellagrous patients. It is not thus in the Tyrol; in fact, Dalla Rosa found at Trente that almost half of his cases had albuminuria. The urines of the pellagrous give on the addition of sulphuric acid a pronounced reaction of urochrome. The sediment of the urines of pellagra patients is composed of the following substances in the order of their frequency: triple phosphates, urate of ammonium, calcium oxalate, sodium urate and uric acid. This preponderance of alkaline salts explains the frequent alkalinity of urine.

A female patient of Régis refused food for a time, but later she ate voraciously, while at the same time she had a diarrhea. Here are two analyses of her urine:

Quantity in liters.. . . .	0.148	0.450
Specific gravity.. . . .	1.021	1.014
Reaction.. . . .	Acid	Acid
Color.. . . .	Yellow	Yellow
Urea, grams per liter.. . . .	11.40	8.7
Total phosphoric acid (in P. O.)		
grams per liter.. . . .	1.30	0.45
Chloride of sodium, grams per liter.	17.30	13.60

[We have found indican almost constantly in the urine, and albuminuria has not been rare in our experience. J. J. Watson, examining the urine of 12 patients 180 times, found indican present 175 times.]

*Typhoid Pellagra:* In considering this very grave complication, so peculiar to pellagra, it is necessary to avoid confusing it in any way with typhoid fever, as was done by Lussana.

The earlier physicians, particularly Nardi, showed that there exist notable differences between typhoid

fever and typhoid pellagra. The latter has no prodromal symptoms and its course is much shorter; it affects the more robust; it has no rose spots; rarely ends in recovery; is always accompanied by a loss of strength proportional to the duration of the malady; and many times, rather than the appearance of new symptoms, presents an aggravation of existing phenomena. Finally, there is wanting in typhoid pellagra, as Verga pointed out in a letter to Billod, the changes in Peyer's patches and Brunner's follicles; furthermore, the spleen is not only not enlarged, but is often smaller than normal.

There are, moreover, still more notable differences in the symptomatology. In the beginning of the disease in these cases one sees not only the dry tongue, prostration, muttering delirium, carphologia, subsulti, intense thirst and the tremor of typhoid fever, but furthermore, strong retraction of the head, epileptiform or tetanic attacks, staring and brilliant eyes, paralysis of the bladder, edema of the extremities, dysphagia, stupor, vomiting, refusal of food, especially meat, or wolfish voracity—all lacking or rare in typhoid fever; also an inveterate diarrhoea with ammoniacal odor and the same odor in the sweat and breath; urine alkaline or neutral, with low specific gravity; and a temperature of 39 to 42 degrees, which is manifested frequently in the first days of the illness, while in typhoid fever the temperature reaches its maximum in the second week.

Belmondo, who has made a special study of this condition, says: "It is rare that typhoid pellagra





develops suddenly, for, as a rule, the ordinary symptoms of pellagra show a characteristic intensity; the enteritis and the nervous phenomena (neurasthenia and paresis) as well as the general weakness assume an unwonted importance, and even on the psychic side there are a clouding of consciousness, depressed tone and a tendency to suicide.

"Most of the cases are poorly nourished and at times much emaciated; however, there are others in which the panniculus adiposus is abundant and the general development of the muscles remains almost normal. There is often almost absolute unconsciousness; at times, verbigeration, or visual hallucinations of a terrifying nature; if the patient is still able to express himself he believes he is surrounded by tormenting flames, (sometimes, also, there is even a true erythropsia), or feeling himself falling from a great height, he crouches in desperation on his bed praying for relief.

"The entire musculature is in a very pronounced state of tonic contraction, and there is marked rigidity evident on making passive movements of the extremities. In these manifestations the reflex rigidity increases and generally the passive movements ultimately become impossible. Often the patient makes spontaneous, incoordinate movements, especially with the hands and arms from time to time. In these movements, apparently intentional, there is shown frequently a tremor of the upper extremities with wide oscillations and a certain grade of ataxia. The speech is drawling, the voice trembling and often nasal.

"The face has a rigid and contracted appearance; however, at intervals the mimic muscles, principally those of the mouth, are agitated by tremors which spread from one muscular fasciculus to another and reach even distant muscles.

"The lower extremities are habitually in forced extension, the feet in plantar flexion. The exaggeration of the reflexes increases up to the last hour of life, the knee jerks being especially exaggerated. Even a definite ankle clonus is not rare. Under a light percussion on the tendon of the quadriceps there is often a spasmodic reaction of the leg accompanied by convulsive movements of the whole body. At times, together with the plantar clonus, there is a paradoxical contraction of the extensors of the foot, and hyperesthesia to factile stimuli so marked that a breath of air or a ray of light may provoke motor disorders or tonic convulsions."

Typhoid pellagra differs from typhoid fever notably by the frequent presence of a large number of cylinders in the urine and the appearance of a large quantity of urea in the blood.

Vassale has drawn attention to the great frequency in pellagrins of a form of chronic parenchymatous nephritis, which is marked by desquamation, tubular degeneration and numerous cylinders. In six cases of typhoid pellagra he found, besides the renal alterations, visceral congestions and enlargement of the mesenteric glands, also a streptococcic bronchopneumonia.

More important still, Belmondo, in twenty cases of typhoid pellagra, found cerebral and spinal

meningeal injection with infiltration by leucocytes, and extensive punctate hemorrhages in the cord; also many degenerated fibers in the cord, with the usual degeneration of the crossed pyramidal tract—lesions more common to meningitis and myelitis.

From all this the conclusion may be drawn that the symptoms of typhoid pellagra resemble the symptoms of tetanus in the general increase of the reflexes and the spastic-tonic convulsions; typhoid pellagra seems, then, to be an acute exacerbation of the ordinary spinal lesions of pellagra. This exacerbation can be attributed sometimes to uremic complications, or sometimes to an associated infection; but, above all, to an intensive influence of the poisons of corn on the spinal cord, either by cumulative effect, by greater quantity, or by higher toxicity of the material ingested. The pathogenesis, therefore, of the fatal tetanic state which can be produced in animals by subcutaneous or internal administration of certain preparations of corn, is in accord with the symptoms of pellagra, which may be typhoidal or may be more attenuated.

The uremic complication of typhoid pellagra presents symptoms allied to those of renal disease rather than of typhoid fever; for example, diarrhea, vomiting, refusal of food, ammoniacal odor, somnolence and epileptiform attacks. But the quantity of albumen in the urine in these cases is frequently very small, so that the diagnostician should be on his guard. In some cases the symptoms of typhoid pellagra are not caused by urea, but by ammoniacal products in the blood, and for this reason they are

marked by diarrhea, paresis, ammoniacal perspiration and alkaline urine.

[We have observed in South Carolina this classical picture of typhoid pellagra occasionally; and we have also seen other grave, acute manifestations, (acute delirium) usually ending fatally, but usually without the convulsive phenomena. This has already been discussed elsewhere.]

*Motility and General Sensibility:* Anomalies of the functions of the muscular system, especially muscular weakness, form in the early stage a part of the classic symptomatology of confirmed pellagra. By the dynamometer one obtains, on an average, 27 kilograms in the case of men (50 cases) and 19 kilograms in the case of women (50 cases). However, in three cases of chronic pellagra in men the dynamometer marked 40 kilograms, and two women brought it up to 35, figures in accord with the normal. Therefore, it is evident that one would not be able to base a clinical diagnosis of pellagra absolutely upon the diminution of muscular force. There are, too, cases in men, robust and advanced in years, who show, apparently, at the beginning of the malady increased muscular power; but this is a subjective feeling which it is necessary to verify with the dynamometer. One really meets with pellagrins, who not only appear in good health but who endure the hardest work of the fields. Still, as Belmondo remarks, often when the strength of the arms persists there is paresis of the legs. The collected anamneses agree almost entirely in emphasizing the nervous symptoms which, after the appearance of



the erythema and of the diarrhea, are observed in the pellagrous, and are manifested by great feebleness of the lower extremities. Tonnini says that the paresis of the pellagrous never attacks the muscles of respiration or those of the face alone.

*Spastic Paresis:* In pellagra in an advanced stage there are two particularly striking symptoms: a very frequent extreme paresis of the lower extremities which is in strong contrast with the increase of muscular tone and reflex musculo-tendinous excitability. It is a true spastic paresis.

*Tremor:* "Tremor occurs in pellagrins," says Strambio. According to Belmondo, there is intention tremor like that of disseminated sclerosis, more marked in the upper extremities, particularly in the fingers, than in the lower. At the same time, there is a lack of co-ordination made apparent by uncertainty upon standing with closed eyes. In the lower extremities these symptoms are less accentuated. In all cases it is more difficult to determine because of the contemporaneous paresis and reflex muscular rigidity. Sometimes there is tremor of the head and of the tongue as well.

*Contractures:* In general there is in the movements and the attitude of the pellagrous a tendency to certain contractures; many of these patients when they wish to rise do so with great difficulty, or wishing to extend the arm it remains rigid and semi-flexed. Many are accustomed to remain constantly drawn up. They squat down, the knees pressed against the chest and abdomen, clinging to some

object with hands or feet or even with the teeth. Often these grotesque attitudes bring stigmata and characteristic deformities.

In the case of one woman the skin was cadaverous and covered with telangiectases, the chestnut brown hair scattered over with white and reddish spots, a rude beard, cranium ultra-brachycephalic, nose flat, teeth of the upper jaw worn away by constant friction, and from this cause, doubtless, a varicose nodule had formed on the tip of the tongue; emotional reaction was feeble, but not abolished; tactile and painful sensibility was very much diminished; she was resistant; mentally she presented the picture of dementia precox of the depressed type and was mute; hid herself in fear in the most retired corners of the room or yard; if any one succeeded in making her talk, she did not seem to be deluded but begged others about her to have pity on her misery, and was grateful for attentions received, of which she thought herself unworthy. All her inclinations and all her psychic activity expressed themselves in the most extreme muscular contractions. She sought the most favorable positions for contortions while hanging to slats and bars to which she clung even with the teeth, the tongue and toes. She gave as an explanation that she could not do otherwise. These symptoms continued up to her death, from tuberculosis, although in the last few days she uttered monosyllables—"good, bad, your kindness, so much misery, etc." But up to the last day she continued to conceal herself as much as possible under the cover and to cling with her feet to the bars of the bed.



**MUSCULAR SPASMS AND TETANIC CONVULSIONS.**  
It is comparatively rare to see in pellagra a partial chorea or that peculiar tendency of running in a straight line, but it does occur, more especially in the morning hours; there is then something which reminds one of epilepsy with ambulatory automatism. Besides, epileptiform attacks themselves are not rare.

In typhoid pellagra there are contractions alternating with clonic spasms of the face and the extremities; they remind one of electric chorea or tetanus and are provoked and aggravated by sensory impressions.

A very common phenomenon, especially in summer, is that of pellagrins falling forward, backward or sidewise in consequence of vertigo and of sudden tetanic movements, such attacks being called by the people "pellagra spells." Calderini reported cases of vertigo in 75 per cent. of the men and 77 per cent. of the women.

General tonic spasms with trismus and subsultus appear under the influence of light tactile stimuli in many patients, just as in experimental animals. The opening or shutting of a door, the noise of an electric bell will sometimes provoke these spells. In one case tetanic rigidity persisted even during sleep, with elevation of temperature to 39 and 41 degrees. As long as they walk and eat patients have the sensation of a cord stretched across the back which draws them forward or to the side and they bend in that direction. These attacks, because light and fleeting, might be called opisthotonic, emprostho-

tonic and pleurosthotonic tetanus. "The convulsions often have the appearance of tetanus," says Allioni. Often contractures of flexion and extension result from them; some of them extend their arms in the form of a cross and remain rigid from four to six minutes; others remain whole weeks with the limbs extended and rigid, like katatonics; others have the sensation of a force which draws them by the head or obliges them to stiffen out the legs (Nardi).

*Tendinous Phenomena.* The patellar reflexes, as observed by Roncoroni, were always rather exaggerated than feeble, as also reported by Alpago, Raggi and others. Out of 146 cases the knee jerks were exaggerated in 65 cases and feeble or absent in 30 cases, normal in 50 cases. The exaggeration is also observed in dogs treated with the poison of corn and differentiates pellagra from ergotism.

Tuczek found among 300 pellagrins the knee jerks exaggerated 200 times; in 23 there was at the same time ankle clonus; in the others these peculiarities were wanting. Frequently there was a difference in the two sides. In the third period of the disease, according to Tonnini, the knee jerks are absent in 10 per cent., feeble in 15 per cent., marked in 25 per cent. Foot clonus was wanting in 30 per cent., was normal in 47 per cent., and exaggerated in 22 per cent. In 42 pellagrins, at other stages of the disease, the knee phenomenon was wanting in two cases, weak in three, exaggerated in six; clonus was wanting in 8; it existed without exaggeration in 28, and was exaggerated in 6.



The reflexes of the skin which Roncoroni studied in 8 pellagrins were normal in 2, elevated in 5 and absent in 1. The pharyngeal reflex in the same individuals was weak in 5, normal in 2 and lacking in 1. In nine other cases the cremasteric reflex was wanting in 3, weak in 3, active in 1, and exaggerated in 2 on the right side only. Foot clonus was wanting in 7 out of 9, lightly present in 1, and very active in another.

On palpation the muscles of the lower extremities exhibit a wooden firmness, with resistance to passive movements.

The mechanical excitability of the muscles is also increased, and often there are idiomuscular contractions.

#### ELECTRIC REACTION OF THE MUSCLES AND NERVES.

This has been studied with Roncoroni in four pellagrins, who had been for some years in the hospital of Turin, of whom three were in good physical condition. They did not display the reaction of degeneration and did not show any deviation, either quantitative or qualitative, from the normal. In one case only the electric excitability was notably less than in the others, which was probably due to profound denutrition. This is not without interest for differential diagnosis from polyneuritis, progressive muscular atrophy, lateral amyotrophic sclerosis, transverse myelitis, and other diseases.

The reaction of the flexors of the forearm is often greater than that of the extensors, as well for K. C. and An. C. as for faradic stimulation; rarely it is the same or lessened. The difference of one side over

the other is not more than 0.4 milliamperes for the galvanic and 6 milliamperes for faradic irritation.

Tonnini also found a greater faradic excitability of the flexors. According to him a diminution of the faradic excitability even in the cases of spastic rigidity is found also in the third period of pellagra; under certain circumstances this reaction might serve as a differential diagnostic sign from spastic spinal paralysis.

*Dysphagia:* Dysphagia is met with in about 2 per cent. of the cases. It is less rare in dogs under experimentation. Tonnini has found numerous cases of hysterical globus, and cites the case of a woman, who, when she swallowed, had the sensation of a live coal. Strambio mentions something similar, and this seems to be observed also in dogs, although their symptoms are difficult of interpretation.

*Gait:* Belmondo found the gait of pellagrins slow and uncertain. Often, he states, the pellagrous walk with short steps, the knees half bent, the legs apart for a larger base of support. In severe cases, walking is not possible without the aid of a stick or the support of other persons. The sole of the foot is scarcely raised above the earth, and often the feet do not even leave the ground, and then, too, one observes the typical spastic paralytic gait. Roncoroni, in his observations on fourteen cases, has not found these peculiarities. From his table it is seen that:

1st. The length of the step in its active part is greater on the left side in ten out of fourteen pella-



grins, and greater on the right side in the four others.

2nd. The length of the step, from the median line, is greater than the normal in eight cases; less in five cases. In one case greater on the right; much less on the left; in six cases the left foot deviated more than the right; while in seven cases the right foot deviates further; in a single case the variation from the median line was equal on the two sides.

3d. The difference between the bilateral deviations is often notably greater than the normal; it is greater on the right in six cases and on the left in seven.

In the greatest number of cases, however, the walk of the pellagrins is not sensibly changed; the tracks are normal, the step regular. The deviation from the median line generally differs little from the normal. But often the deviation is not complete on the two sides in a series of steps.

#### SENSIBILITY TO TOUCH AND TO PAIN.

Sensibility is often abnormal among pellagrins. The observations of Albertotti on thirty cases gave the following results with the esthesiometer:

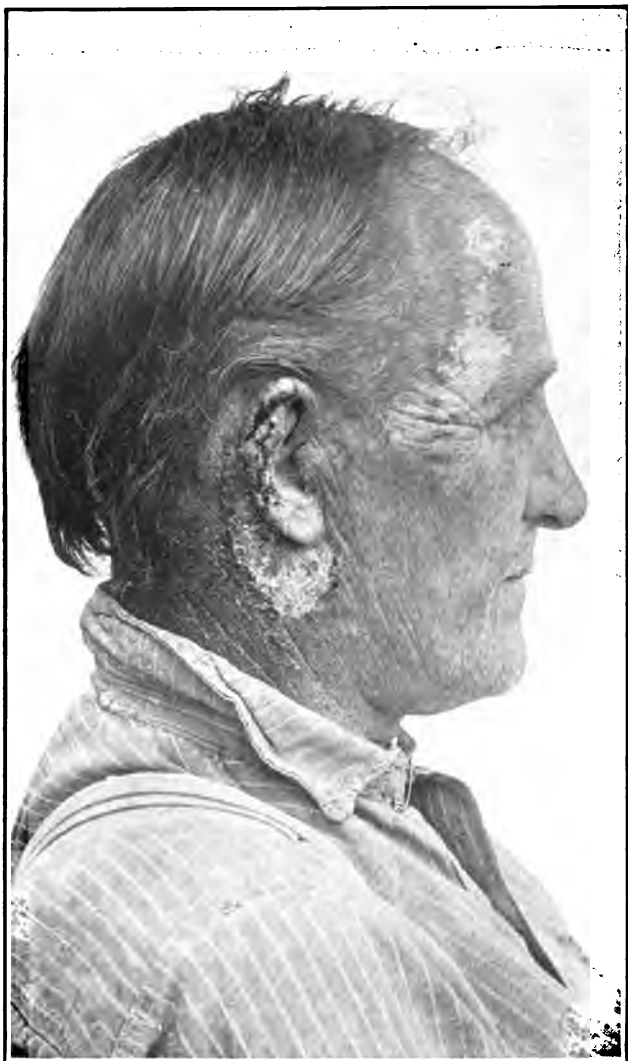
End of the finger: Separation, 2.2 mm. (normal 2.1 mm.)

Forehead: 15 mm. (normal 8.8 mm.)

Back of the neck: 21 mm. (normal 10 mm.)

Back of the hand: 28 mm. (normal 19.5 mm.)

Roncoroni found in 12 cases of pellagra, as an average, at the end of the fingers, on the right side,



**Plate XIV. Illinois case. Unusual localization involving mastoid and frontal regions; bilateral. Courtesy of Dr. G. A. Zeller.**





2.70 mm.; on the left, 2.85 mm.; on the tongue 1.55 millimetres. Tonnini found a diminution of the sensibility of touch in ten out of thirty severe cases.

The experiments on the sensibility to pain by the faradic current induced by Lombroso's method were made in individuals in whom there was no trace of erythema, and it was diminished principally on the hands and on the back of the neck. Thus, while healthy males show signs of pain in the palm at a distance of 43 cm., from the Ruhmkorff coil, and females at 60 cm., the pellagrous scarcely display pain in the palm at from 20 to 47 cm.

Tonnini, in a similar series of experiments by Lombroso's method, obtained analogous results, as shown in the table below.

Parts of Body	Average Normal	Average Pellagrous	Differences
Ends of fingers. . . . .	54	35	19
Forearm (internal surface). . . .	59	41	18
Forearm (external surface). . . .	60	35	25
Forehead. . . . .	92	90	2
Nose. . . . .	94	90	4
Palms. . . . .	46	29	17
Back of hand. . . . .	54	39	15

The diminution of the sensibility to pain observed among pellagrins is not found in the other insane, among whom it is generally increased, or, at least, normal.

Out of thirty severe cases, Tonnini found five times a profound analgesia extending from the feet

even to the face, but greater in the lower extremities; he found more or less analgesia fourteen times, and hyperalgesia four times. In forty pellagrins less severely affected Tonnini found two-thirds analgesic, and only two hyperalgesic.

Hyperalgesia in pellagra is more common in florid types, and is accompanied by a decided elevation of the temperature. The cases are numerous in which, if they are touched, principally on the stomach or on the thorax, they begin to cry out, and at the least noise they start; others have painful paræsthesiæ, as if water were thrown on their heads, or as if they were pricked on the legs by thousands of pins; they complain also of burning in the eyes, in the nose and in the face. Insensibility to pain is often shown by their voluntary exposure to cold as well as to burning or scorching to which they repeatedly expose themselves. Tonnini found the sensibility to heat better preserved in the face than in the extremities. But sometimes cryesthesia is found.

#### VISION.

In five cases of pellagra observed by Roncoroni and Ottolenghi the sight was normal. Among ten the study of the visual field did not disclose anything worthy of note. In two other cases there was partial vertical homonymous hemiopsia. In five cases color vision was entirely normal.

#### TASTE AND SMELL.

The sense of taste is little diminished; four pellagrins being examined with strychnine sulphate

could, on the average, detect the bitter taste in a 1 to 243,000 solution (healthy individuals 1 to 500,000). Saccharine was detected in solution of 1 to 37,000 (healthy individuals 1 to 80,000). These same persons noticed perfumes in very dilute solutions (1 part of oil of carnations to 50,000 of water). They distinguished readily also quantitative differences in solutions of perfumes but could not describe their nature.

#### ANOMALIES OF SENSATION.

A subjective sensation experienced with few exceptions always in the beginning of the disease, and lasting frequently to the end, is that of burning on the hands and legs, sometimes over the entire body. Others, on the contrary, experience a sensation of cold or of heat internally and of cold in the extremities.

Then there is frequently pruritus in the groin or on the back and arms; some patients have abnormal sensations in the genital organs and in the anus, just as do some alcoholics; others believe that they feel hot water running down the back, or on the head, or have burning and itching at the nipples and in the inguinal region; when they are touched they think they feel prickings and twitchings, principally between the shoulder blades, in the thumb and on the soles of the feet. Sometimes this sensation extends all along the vertebral column, so that the patients cannot be covered in bed or dressed without great distress. Often they feel neuralgic pains in the arms, in the groin or in the thighs, and shoot-



ing pains which injections of morphine do not relieve.

Frequent are the cases of cephalalgia, which increases if the sick remain on their feet or are exposed to the light of the sun. Once persistent hemicrania was noted, with increase of temperature on one side of the face and enlargement of the pupil of the same side.

An intelligent female pellagrin, subject to frequent attacks of crying and continuous insomnia in the five or six days which preceded these attacks, had an invincible desire to sleep. Another lay down in the fields in order to sleep, and remained thus two or three days; she became angry when they wished to interrupt her sleep. This somnolence is sometimes persistent, and in one case it lasted two years. Insomnia, however, is more common even among pellagrins not mentally affected.

## CHAPTER VII

### PSYCHIC AND PARETIC PHENOMENA, COMPLICATIONS, HEREDITY.

It is not easy in the study of the psychic phenomena of pellagra to distinguish those symptoms produced directly by the disease from mere coincidences or accidental complications, more especially insanity. There are depressed mental states which arise from the pitiful and wretched condition of these pariahs of upper Italy. This condition can frequently be explained as a melancholia analogous to the melancholia *ab miseria* of Laségue.

A notable peculiarity among pellagrins, even when not mentally affected, is an increasing irritability; at the least inconvenience or on the slightest emotional disturbance they quickly display temper, although ordinarily they appear quite normal.

This is a characteristic common to alcoholics and to paralytics in the early stages of their malady; and this can be explained by the law that any enfeebled organ is readily irritated and easily suffers. The laity, who consider these external signs only, frequently attribute pellagra to moral causes. Perversions of feeling are generally rare.

Very often the patients complain of a loss of memory and of mental weakness, which diminish when they are in bed or lying down. Certain others indulge in introspection and analyze very acutely their mental troubles. The poor wife of a fisherman, ordinarily taciturn and apparently rather dull,



caused surprise in the course of her attacks by some rather remarkable observations, for instance: "Notice, now, these invalids, they have no hearts, they are full of superstitions, they use cards to learn whether their husbands will be true, as if the chance of cards could have such influence; then from the accidental fall of a card they draw conclusions by which they are irritated and plunged into quarrels. Is not this sickness rather than insanity?"

Chronic pellagra is often accompanied by a hypomaniacal state with a tendency to sarcastic speeches and caustic observations, a thing often seen among other insanities. Frequently the pellagrous psychosis appears under the form of a special melancholia, more often in the form of an insanity with systematized delusions. This last form may be observed in hereditary pellagra; vagaries of memory, self-accusations, nosophobia, apprehensions of personal violence, delusions of pregnancy, loss of personality, and concealment of sex have all been noted.

A woman of Seronno, 38 years old, confided mysteriously to the judge that she had been violated and had become pregnant. She believed that she had given birth to a child, and then, with the help of her seducer, had buried it alive; for three months she led the officers of justice to many places in search of the little corpse; when finally a medical examination revealed that she was a virgin suffering from pellagra.

In another case a male pellagrin imagined himself affected with venereal disease. He dosed himself

with remedies advertised in the newspapers, and at last complaining that all the world was pointing the finger of scorn at him, he threw himself into the water.

Another sufferer, of sufficient intelligence to be employed in the care and instruction of convalescents, imagined that he was going to marry in a short time a young and wealthy marchioness, and dissimulated his delusion with a finesse which is sometimes seen in the paranoiac state.

A pellagrin in the hospital at Milan, besides the usual symptoms of pellagra, suffered from a cardiac affection accompanied by edema; he displayed a true monomania of avarice, rigidly economizing his own food, at the same time striving to prevent others from eating.

But these are exceptional cases, and, as Verga has noted, are probably only examples of a psychosis engrafted upon pellagra.

In general, even when pellagrous mania assumes a type, it is rather that of systematized delirium than of paranoia.

In almost all cases of pseudo-monomania there is associated a well nourished body, and this is another analogy with general paralysis.

Another characteristic in pellagrous insanity, is a real or, more often, apparent stupidity or an obstinate mutism. The sick stay motionless in a crouched position, as if they sought to avoid not only social contact with other people, but even the light itself. When this apathy ceases, it may be succeeded by attacks of psychic epilepsy or often followed by an

active delirium ending in a ceaseless torrent of words. In other cases, instead of these depressed and sluggish phenomena, there may be observed a persistent gaiety or an exaggerated activity. The patients repeat, without weariness, certain appeals, chants, phrases, sometimes with an insupportable tenacity, and resemble in this the stereotypy of dementia precox.

Cases of hallucination are numerous, especially those having a strain of cenesthesia, and these have a certain dependence upon an abnormal state of the viscera. They burn, they have dogs in their stomach, they see water on all sides, and hear voices commanding them to drown themselves; or, perhaps, they are aggressive, believing themselves insulted. The psychoses of pellagra do not show persistent paroxysms without interruption, they are rather short recrudescences and fleeting disturbances.

The anarthria or brief aphasic attacks which are found in certain paralytics, alcoholics or epileptics, are not met with in pellagra. There is, however, often an embarrassment of speech with a tendency to repeat certain words, and to pronounce phrases without connection. Two peculiarities which are more characteristic of pellagrous psychosis are sitophobia and hydromania.

The most frequent form of psychosis in pellagra, according to Régis, is mental confusion with depressive states or with delirium. It exists, more or less marked, in most of the cases. It manifests itself by inertia, passivity, indifference, torpor, frequently very marked; by insomnia, often with terrifying

hallucinations both of sight and hearing; by depressed delusional states with fixed ideas of despair, of damnation, of fear, of anxiety, of persecution, of poisoning, of possession by demons and sorcerers (Warnock); by refusal of food, and a tendency to suicide, especially to suicide by drowning, so much so that Strambio has designated this feature of the disease by the name of hydromania. This melancholic depression, which may go in certain cases as far as stupor, is always accompanied by, or founded on, a certain mental obtuseness, even intellectual dullness, and considerable general anesthesia (Morichon, Beauchamp and Courtellemont), which finally becomes permanent and culminates gradually in a dementia which deepens in proportion as the pellagrous cachexia progresses. It may be accompanied by polyneuritis (Righetti).

One may observe also in every severe chronic intoxication a morbid state resembling general paralysis (pellagrous pseudo-paresis). This occurs especially in those cases in which, instead of the habitual melancholic ideas, the patients present ideas of satisfaction and wealth (Warnock, Marie).

"Stupor," says Girma, "has been often mentioned, as well as ideas of suicide; in two cases the disease developed with alternations of agitation and depression; twice there was an intellectual torpor, like dementia; three times trembling of the hands and of the tongue was noted, as well as difficulties in walking, difficulties of speech, and once paraplegia; these cases furnished a symptomatology somewhat similar to that of paralysis and we even make use of

the term *pellagrous pseudo-general-paralysis*; once there were spinal and abdominal pains.

"Deaths in pellagra have resulted: three times from cerebral congestion; four times from pellagrous marasmus with diarrhoea; four times from pulmonary tuberculosis. These deaths followed upon a rather short stay—some months at the most—in the Asylum of Pau.

"The cases which recovered progressed favorably rather than rapidly under a tonic regimen and their discharge took place in the course of the first year. Only two hereditary cases, with mental aberration, had to be detained longer; one developed dementia; the other, originally defective, was discharged at the end of three years 'improved.'"

#### REFUSAL OF FOOD.

In many cases refusal of food is the result of perverted innervation of the stomach, which shows itself by anorexia or voracious appetite. Such patients often say they feel a lump in the epigastrium, and cannot swallow food (dysphagia). A female patient obstinately refused all nourishment during her insanity, and upon recovery ate on request, but with great repugnance. "It seems to me that I am filling up a body already full; I am full up to the neck." Constipation may sometimes explain this sensation of repletion. Repugnance for food may also be explained by other somatic causes or delusional ideas—fear of injury, of indignity, of culpability, etc. In other cases it may be due to hallucinations, such as visions of the host on plates

or fear of poison, but it is then only a partial sitophobia. Repugnance to food is sometimes due to negativism and resistance; if no notice is taken of such patients and they are left to themselves, they eat better.

#### SUICIDE.

The other condition, characteristic of pellagra, hydromania, has also variable and complex causes. In many cases there exists a real passion for water; and this is justified by the continuous burning sensations which are relieved by effusions of cold water. "See," said a patient, "this water is my only salvation, if I were not able to bathe myself constantly these burning sensations would drive me to suicide. I would not give this water for all the treasures in the world." In rigorous winter weather some may even break the ice in order to plunge into the water. In other cases this tendency does not spring from sensations of burning, but seems due to the pleasure evoked in patients by the attraction of the shimmering surface of the water. This peculiarity is related to certain modifications in the retina, and is seen at times in children and in some paralytics.

On some pellagrins fire produces impressions similar to those of water; they may throw their effects into it, and even burn their own hair or beard. A gardener, forty-five years old, who suffered from pellagra with pruritus and a muscular feebleness, which compelled him to rest at least two days each week, used to say: "Nothing in the world gives me more pleasure than a little stream; when I take a walk I go alongside of it and look at it always as





long as I can. In the night I dream of seeing water."

On the other hand, others have a great repugnance to water; the sight of it terrifies them. This repugnance is poorly interpreted by many observers. It may lead to suicide by drowning from a paradoxical attraction against which, at first, the patients try to struggle. For an accurate comprehension of this phenomenon it is necessary to analyze their confessions. "When I see water," said one patient, "my eyes are blinded and I am nauseated. If I cross a bridge, I am obliged to close my eyes, and try to walk in the middle, otherwise I should fall." "If I look into the water," said another, "I am obliged to close my eyes, and to hold on to a stake or to a tree; if I do not, I feel myself attracted by the water and am likely to fall." "If I do not close my eyes at sight of water, it forces me to turn my head in its direction, and I cannot withdraw my gaze from it," etc.

These two contradictory phenomena of attraction and fear are really not irreconcilable. Certain of these "hydrophobias" are marked by a fear of flowing surfaces because of photophobia. For others, however, actual contact is sometimes necessary, while still others cannot endure to drink any but hot liquids or the opposite.

These sufferers certainly do not go into the water because of any predilection for it, quite the contrary. Indeed, water, as does a mirror in certain delicate women, causes in some an overwhelming impression of disgust, or of repugnance or a vertigo.

One day, in fine weather, a patient being placed in front of a turning mirror, hid his eyes, drew back his head, and did not wish to look again, saying that it produced on him the same effect as water. Another patient, when placed before a mirror which reflected the rays of the sun, fell a few minutes afterwards in an attack and was nauseated. Many patients have a repugnance for water, notwithstanding the fact that it does not cause them to feel stupefied. Here again is seen evidence of the contradictory phenomena which are so often found in chronic intoxications, especially in pellagra. Some even feel repugnance to cold water, and are obliged to heat it in order to drink. In Tuscany, pellagra is often the cause of many people not being able to endure hydrotherapeutic treatment.

Many sufferers drown themselves not from disgust of life, but in obedience to hallucinations which probably arise in recollections of former agreeable impressions, associated with water.

Suicides by drowning are numerous also by reason of a kind of motor automatism or instinctive impulsion, similar to attacks in epileptics. They do not know why they throw themselves into the water, and if they survive, they can not explain their attempt.

Certain patients throw themselves into the water not to drown themselves, but to find some relief from their torturing paresthesias, and being seized with vertigo, they are drowned. One pellagrino could neither go to stool nor urinate anywhere except in a ditch, the water of which alone could stimulate his enfeebled reflexes.



Finally, frequent suicides occur from a fixed resolution to escape from the sufferings of the malady. In the execution of their attempts they derive aid from a profound perversion of sensibility, which, while it makes them painfully aware of certain impressions, arising from the stomach and heart, renders them, on the other hand, less sensitive to trauma and other more painful things. Thus a pellagrin, who suffered intolerable pains in the epigastrium, cut his throat with a sickle, and then dragged himself 100 metres to his house with his sickle in his hand.

It appears, then, that when death by drowning occurs among pellagrins, there is always doubt as to whether it is accidental or suicidal.

Statistics show that in those provinces of Italy where pellagra is prevalent, suicides by drowning, voluntary or accidental, are more numerous than in the provinces whose inhabitants, by the nature of their work, or by the mere situation of their habitation near the water (Naples, Sardinia, Liguria), are more exposed to drowning. It follows that in districts like Lombardy and Emilia, where there is much pellagra, almost half of the suicides occur by drowning. On the contrary, Tuscany, Romagna, Naples and Sicily, which have a numerous population of fishermen, and are half surrounded by the sea, have a small number of such suicides in comparison to population.

These facts would become still more obvious if the deaths by accident are compared with those by drowning in various regions or provinces, though there are exceptions.

## INTERMISSIONS.

A remarkable peculiarity of pellagra, that is well known, is the intermittent appearance of the psychic symptoms.

The rare attacks during cold weather are almost doubled in the months of spring. They become particularly numerous in the month of March, and increase with the heat up to July. The number is small in the spring and increases again in autumn (September).

For more exact observation a record was kept of severe psychic exacerbations in 100 pellagrous insane during a period of five years; the averages are given in the table below :

	Dec.	Jan.	Feb.	Mch.	April	May	June	July	Aug.	Sept.	Oct.	Nov.
Attacks.....	33	34	27	50	54	67	77	88	46	81	66	48

There are two causes for this. The influence of the elevation of temperature, but still more, the rapid thermometric and barometric changes. The attacks of autumn are those which demonstrate this. Other observers, as Calderini, have remarked that in many cases of pellagra, the relapse of psychic troubles took place in the autumn instead of in the spring.

Spring recrudescences are also observed in endemic alcoholism. It is possible that these symptoms depend on the deficiency of certain mineral salts in the blood, for example the phosphates, which are diminished in the first cold months, more exactly in the proportion of 0.569 to 1.064, in comparison with the winter months.

In six cases a tertian type of recrudescence was noted. For example, M. G., thirty-seven years old, refused nourishment for a day, pulse 90 and temperature 37.5 C. degrees; the following day she was entirely herself, pulse 80 and temperature 36; the third day she was delirious again, with increased temperature and pulse rate.

Another periodicity common in pellagra is of a diurnal type with recrudescences at certain hours. Almost all the patients say that their headaches are more violent between midday and three o'clock, during the hours of the greatest heat. Others declare that they have vertigo all night, and hallucinations before falling asleep, whereas during the day they feel well.

#### DEVELOPMENT.

From the standpoint of the evolution of the individual, certain pellagrous psychoses are characterized by an arrest of development (denied by Ferrario); a kind of hebephrenia with genital and general insufficiency; numerous examples of this have been cited (hereditary pellagra and infantile degenerations).

#### COMPLICATIONS.

Pellagra may be complicated with many other diseases, which sometimes mask it completely. The most common of these is alcoholism.

#### (A) ALCOHOLISM.

The question whether certain symptoms come from alcoholism or from pellagra, is, at times, very



Plate XV. Illinois case. Marked symmetry of all lesions. Courtesy of Dr. G. A. Zeller.





difficult to decide. This arises in part from the fact that many incipient pellagrins, like paralytics, seek a passing solace in alcohol. Others are obliged by their expenditures in alcohol, to buy for food spoiled corn, which is, of course, cheaper.

Small quantities of alcohol used by others, already predisposed to the disease by the poisons of corn, easily precipitate the malady just as might be done by other secondary causes. These two factors are often coincident, and the sufferer, not willing to confess his vice, leads the physician into error.

A pellagrin of Verona said he made from five to six francs per day as workman in a factory, and was obliged to quit his work because of his malady; he was, as a matter of fact, sent away for drunkenness and was obliged to beg his bread; he was a hardened drinker who sold the bread he begged in order to buy brandy and spoiled polenta. Since then he has suffered from muscular feebleness, trembling, diarrhea, pruritis, epileptic attacks, weakness, want of appetite and dilatation of the capillary vessels of the face.

Another drunkard, who also ate spoiled polenta in order to be able to procure brandy, suffered, at fifty-four years of age, with severe headaches, marked feebleness of the legs, vertigo, constipation, desquamation of the hands, burning pains on the soles of the feet, and, later, ptosis, trembling and convulsions of the right hand with slow pulse and atheroma.

The Piedmont Commission, as well as Paolini at Bologna, noted frequently the coincidence of pellagra and alcoholism. It is remarkable, however, that in the years of rich wine harvests pellagra is rare. This contradiction disappears when one recalls that small quantities of wine are helpful, while large quantities are injurious; and



that a lack of wine in many places means an absence of prosperity, and the necessity of eating poor corn. In general the cases in which alcoholism and pellagra are coincident seem less severe than those of pellagra alone; and all of these cases have been found in the cities.

[According to Nicolas and Jambon, three classes of persons are subject to pellagra: those who eat corn, the insane and alcoholists. A similar idea is entertained by some Italians who call their cases true pellagra in persons who eat corn products, ethylic, in those who use alcohol and mixed in those who use both.]

#### (B) TUBERCULOSIS.

A disease often complicated with pellagra is tuberculosis. It is very rarely found among the pellagrins of Venetia and Lombardy, but Della Rosa found numerous cases of it in the southern Tyrol. He found in fifteen fatal cases of pellagra ten cases of tuberculosis. The rarity of a tuberculous complication in upper Italy has been attributed to an antagonism between tuberculosis and the cardiac affections to which pellagrins are often subject. Perhaps the old writers have confounded tuberculosis with croupous pneumonia, which is frequent in pellagrins, as are also pulmonary edema and emphysema, especially in those with mental alienation.

#### (C) SYPHILIS.

In Roumania, Felix found numerous syphilitic pellagrins, but this complication has not often been found in Italy. It is worthy of note, however, that

syphilis in certain parts of Roumania is very widespread in consequence of insufficient prophylactic measures.

#### (D) THYROID DISEASE.

In the Lombardy districts where goitre and cretinism prevail, pellagra is widely spread; so much so that often relatives and physicians regard the one disease as the cause of the other.

Atrophy of the thyroid gland is met with in the pellagrous, but it is still more frequent in the hereditary cases with arrest of development.

This seems to show the easy vulnerability of this gland to the poisons of corn, and helps to explain the dystrophic and myxedematus phenomena sometimes observed. It may be added that this alteration of the thyroid seems of much consequence in aggravating certain symptoms of the pellagrous intoxication. Pellagrous psychoses accompanied by thyroid disturbances are marked by signs of stupor; sitophobia is also frequent in such cases, and cures are more rare.

#### (E) UTERINE COMPLICATIONS.

Among the numerous complications there are also utero-ovarian diseases, and it is often impossible to distinguish whether these are accidental complications, or are really essential phenomena of the disease. [This subject is more fully discussed elsewhere.]

#### (F) MARASMATIC DEGENERATION.

A very common complication is marasmatic degeneration, and a theory of pellagra has been based on it. The sufferers, especially if poorly nourished, even on full diet waste rapidly, and

finally show a great degree of emaciation, with a reduction in weight even as low as 28 kilograms. This emaciation, however, ceases in the winter months. It is generally accompanied by hydromania, persistent mutism, and rather frequently by hyperinosis.

[Malaria, by some writers, is spoken of as a rather frequent and very important complication of pellagra. It has not been common in our experience even in the southern United States. Wood, from North Carolina, has, however, reported interestingly on this complication.

Hookworms, round worms and other intestinal parasites have, in the South, been very common in our experience; and, of course, add to the gravity of the outlook at times.

The question of intestinal protozoa in pellagrins attracted much attention at the National Conference on Pellagra at Columbia, South Carolina, 1909. Much possible importance was attributed by Siler and Nichols to amebiasis, which they found very frequently present among insane pellagrins in Illinois. Allen also reported the frequent presence of amebæ in the stools of pellagrins in North Carolina, as has Long, in South Carolina and Pennsylvania more recently.

The opinions of these observers generally was that amebiasis should be regarded as a serious complication of pellagra, and that such intestinal protozoa might have important effects by increasing intestinal irritation and modifying the absorption of endogenous toxines. Some recent students of pellagra seem to regard amebæ as a possible cause of the disease.

In our experience, while we have found protozoa not infrequently in the stools of pellagrins, amebiasis has been comparatively rare.]

#### DIAGNOSIS.

So far as concerns the differentiation of true pellagra from alcoholism and from paralysis in its last stages, it is important to note that in pellagra there are wanting marked disturbances of speech; arterial atheroma is rare; the ambitious or melancholic delirium of paralytics is very rare. The urine does not show the density and abundance of phosphates seen in that of alcoholics and paralytics, and the visual and tactile hallucinations of the drunkard do not occur. Alcoholics do not have hydromania nor atrophy of the heart nor the earthy complexion and faces observed in pellagra.

#### HEREDITARY PELLAGRA.

There are, however, forms of pellagra, or of pseudo-pellagra, most difficult to diagnose because the disease does not show itself in its full symptomatology. This is designated as hereditary. Like hereditary syphilis there may be two types, one very severe, another very benign and mild.

The first manifests itself about the second year of life. It is rarely accompanied by desquamation; most often there are epigastric pains, pyrosis, sitophobia, unsteady gait, fears, diarrhea, yellowish complexion, as in malarial cachexia, retardation and arrest of development; later may be seen the com-

plete phenomena of a pellagra which resists all therapy. In some there are noted marked brachycephalia or dolichocephalia, with receding brow, ears badly set, facial asymmetry, anomalies of the genital organs or other physical stigmata of degeneration. In the districts where this form prevails, the benign form is also seen, and merits more study from the prophylactic and hygienic point of view. It is a true "*pellagra sine pellagra*."

Many of these unfortunates are seen in certain sections of Venetia, and of Trentino, even among the well-to-do classes. They complain of burning at the extremities, of pains in the back, and of pyrosis. The women suffer from leucorrhea, uterine heaviness, amenorrhea, flatulence, vertigo, constipation or diarrhea, and a yellowish color of the skin, but desquamative skin lesions and delirium are wanting.

These complications move me more to compassion than does true pellagra, because they indicate how misfortune may occur through hereditary infiltration into the germ of an entire population. It happens with pellagra, as with cretinism, that the disease once scattered in a group of families, predisposed by locality, misery, etc., displays its taint even among families which might have been exempt, bequeathing them, if not the body, at least the livery, as Verga has well said, of this endemic malady. (Lombroso.)

In Favrio it seems undoubted that heredity acts directly. All the alliances of the Franceschinelli and Lorenzi, for example, being afflicted with pellagra,

while the Briosi family, who live with equal parsimony, if not misery, are entirely exempt.

#### ATAVISM.

Many times hereditary influence, on the other hand, is not so evident, for atavism is displayed in the weak attention and the labile memory of the poor peasant, and may be indeed a preponderating force over paternal heredity.

For instance, a young pellagrous girl, 16 years old, suffering from typhoid pellagra, had had chronic diarrhea at the age of two years, and at eight years vertigo, later typhoid pellagra and insanity; she had healthy parents, but her grandfather had died of a pellagrous diarrhea at an advanced age.

In another case a boy of 12 years, of retarded development, with scaphocephalous cranium, suffered from a continuous diarrhea, with a tendency to bite; he also had the habit of striking his head against a wall, indeed so often as to cause an osteoma to form on the left side of the cranium, and he displayed an exaggeration of his sensory and motor reflexes. The father and mother were healthy, intelligent and sound, brothers pellagrous. The grandfather at a certain age, however, suffered from a tendency to bite, and would fall to the ground at the least noise; he also had the habit of beating his head against the wall just as his grandson had.

"The descendant of the pellagrous is recognized by his vacillating and uncertain step; his muddy, yellowish sclerotics, his fixed look, the pale and ashy color of his face, his reddish eyelids, his hare-lip, the scant hair on his head, his brow prematurely furrowed, his flabby muscles, his stupid and apa-

thetic appearance. This general aspect is found in children of ten to twelve years and is the appearance presented by the children of pellagrous parents." (Sacchi.)<sup>1</sup>

The pellagrous intoxication of antecedents, and especially of the pregnant mother, is capable of producing in the offspring early and rapid exhaustion of vitality, degenerative changes and especially arrest of organic development.

In hereditary pellagra there is a very high percentage of mortality. The stigmata of degeneration are common, especially anomalies of the cranium, arrest and retardation of bodily development, even veritable dystrophic infantilism, myxedematous dwarfism, or the exhaustion of the procreative power.

"I remember very well that when wretched, scrofulous children presented themselves at my home, my father would say: 'It is the offspring of a pellagrin.'" (Sacchi.)

Especially prominent among the descendants of old pellagrous families, are peculiar nervous troubles, manifested by sadness, depression, and suicidal tendencies most often carried into execution by hanging. Hereditary pellagra may also be combined with an acquired pellagra.

In France, pellagrous insanity, now almost unknown, still manifests itself under the form of hereditary pellagra, as the recent work of Régis shows. According to the statistics, the asylums of Pau and Montpellier are almost the only ones in

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<sup>1</sup>Piedmont Commission, 1847.

which this affliction exists. This shows that pellagra is only possible where corn is consumed. This cereal must needs enter into the daily food, a thing which happens only exceptionally in France, and then in the back country, among the miserable and desolate.

It is not the same in Spain, where pellagrous intoxication persists in certain regions and affects sometimes even 20 per cent. of the population.

In Italy, in spite of the valiant struggle of Lombroso during all his life, the regions of Bergamo, Brescia, Venice, Padua, still number 35 to 50 pellagrins to 1,000 inhabitants. Treviso, Vicenza, Cremona, Pisa number 10 to 20 each per 1,000. At Milan the writer examined, some months ago, several insane cases of pellagra. The total number of cases in Italy is estimated at 72,000. [The estimate of R. A. C. Wollenberg (op. cit.) July, 1909, of the total number of pellagrins in Italy is less than 50,000.]

In Eastern Europe pellagra prevails, also in Roumania, Servia, Bosnia, Macedonia, Albania and the Turkish countries, as well as in Greece.

The fine work of Babes and Marinesco in Roumania on the neuro-pathology of this intoxication is supplementary to that of the Italian school to which we owe the prophylactic measures of the law of July 21, 1902, which originated in the Anti-pellagra Congresses of Bologna, Padua and Milan. (See Appendix I.)

In Egypt pellagra is spreading as in other Turkish countries, where corn is largely eaten. There, one can say that almost all the fellaheen are, to some



degree, tainted by the poison of pellagra. In the hospital of Kasr el Ainy at Cairo, in ten years more than a thousand pellagrins have been treated. Each year, out of this number, forty cases complicated with mental disease are successively turned over to the asylum of Abbassia, where the writer has been able to study them.

Outside of the hospitals, the study of pellagra among the population of the country districts has been undertaken by Sandwith (Egyptian Congress, p. 485). He makes an average estimate that more than 36 per cent. of the Egyptian peasants are affected. In the less wretched districts the proportion may fall as low as 15 per cent., but elsewhere rises to over 62 per cent.

In lower Egypt the average would be greater, even in young women. The considerable rate of still births would not be properly explained without reference to this scourge.

In upper Egypt the greater dryness and the use of millet as food diminishes the danger; and probably also, the countries further removed from the seacoast consume less imported corn, which is the more dangerous because of spoiling during transportation.

The number of pellagrous insane is continually on the increase; and yet only those are counted who show the definite physical stigmata, such as those whose photographs were presented to the Academy of Medicine in 1907, for the hereditary pellagrins do not always show these stigmata so definitely.

The erythema varies in appearance according to the stage under consideration, though the location may be the same.

Racial characteristics are manifest in relative peculiarities of pigmentation; it is thus that old scars, instead of presenting a dark color, as in case of the white man, show, on the contrary, more of a gray tint in the Arabs, in consequence of the scaly thickness of the dry and hypertrophied skin.

The climate and the Arab costume produce also certain local peculiarities of this erythema; thus the short and large sleeves cause the pellagra gauntlet to be more extended; the *gandoura*, freely open at the breast, cause the dermatitis to extend to the neck and sternal region. (See Frontispiece.) On the legs the boot erythema can extend often above the knee and the bare foot is involved, as is the hand. One can observe either increase of pigmentation at the beginning, or the final depigmentation with a dystrophic state of the epidermis which becomes like parchment, dried and scaly. Scars of old ulcerations frequently occur in these people and make further changes in the aspect of the skin on the most exposed parts.

The ulcerous stage is sometimes preceded by a phase of desquamation which occurs in strips of pigmented epidermis leaving cracks and fissures. We have made various photographs of these different phases. In the negro the erythema, especially on the face, may take the appearance of pigmented grains of millet, apparent on the brow, the neck, the cheeks and around the lips.

It is unnecessary further to discuss either the well-known skin lesions with their seasonal recurrences or the prominent visceral troubles which accompany them (diverse gastro-intestinal troubles, gastralgia, diarrhea, etc.). We will restrict ourselves to the mental and nervous peculiarities, whose manifestations are generally consecutive to the preceding symptoms, although they may precede or even replace them entirely.

The mental state of these patients generally is characterized, after the initial stage of feebleness and irritability, by an apathy with physical and mental depression and diverse phobias. Sitophobia is frequent and coincides with the gastro-intestinal troubles, gastralgia, cramps, nausea, seborrheal condition, constipation and diarrhea.

Mutism is usually associated with sitophobia; the patients become excited and frightened, seclude themselves and seek dark corners (photophobia, hyperthermia, painful, cutaneous paresthesias).

Mental stupor is accompanied by amnesia and by spasms, including vertigo and epileptic convulsions, or their psychic equivalents. In the first rank of the latter phenomena must be noted ambulatory automatism, a frequent cause of unconscious suicide by precipitation into, or drowning in the canals of the Nile.

Autoaccusations or nosophobic, hypochondriac preoccupations are not rare, being associated with vague ideas of persecution. Stupor is interrupted by automatic raptus and various spells with or without confused dreamy states.

Sitophobia may be due to dysphagia and anorexia, and the apathy may be confined to katatonia. It yields sometimes to sitomania at a later phase, for pellagrous insanity frequently assumes the chronic form with or without intermissions. That is easily understood, for convalescent patients returning to a dietary of spoiled corn, the same causes then reproduce their same effects. Relapses are frequent, and the chronic states also; complications, furthermore, through other etiological factors of psychosis are not rare.

In Egypt the pellagrous intoxication at times occurs with hashish intoxication. Then there is the possible combination of various infections, especially of malaria and of syphilis, and such endemic parasitism as ankylostomiasis, which is found very prevalent among Egyptian insane as well as among the native population in general.

With regard to syphilis, attention has already been called to the frequent occurrence of general paralysis among the Egyptian Arabs. The question is, does pellagrous pseudo-general-paralysis exist among them, or is this a simple specific general paralysis modified by the pellagrous intoxication? The question is not a new one, and it was raised by the French school at the time when the academic debates started by Baillarger in 1847,<sup>1</sup> were attracting attention.

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<sup>1</sup>The point was with regard to addressing a programme of inquiry, proposed by Roussel, to the Minister of Commerce—an inquiry to be made in Spain as to the causes and manifestations of pellagra, which was then wide-spread in the southwest of France.

M. Gilbert, member of the Academy, expressed an opinion con-

An examination of the pellagrous lunatics among the Arabs at the asylum in Abbassia show that true pellagra is very frequent among them, as it is among the population from which they come. In addition to the insane who have become pellagrous, there are cases of insanity consecutive to pellagra and in strict causal relation therewith. Such cases show their pellagrous origin by typical phenomena united with characteristic physical stigmata.

A certain number of paralytic insanities coincide with pellagra in their essential phenomena, and confirm the opinion of Baillarger that the ultimate paralytic stage of pellagra may represent a condition identical with paresis both clinically and pathologically. These cases do not weaken in any respect the character of specific general paralysis, from which they are distinct, and which is, of course, ascribed to syphilis. The two forms, however, may be associated, that is, one may observe Arabs suffering from general paralysis who are at the same time syphilitic and pellagrous.

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trary to the corn theory, resting for support on the cases observed by him at Paris in the Hospital Saint Louis.

He probably had before him hereditary pellagra, analogous to the case mentioned by Régis of a patient that had never eaten spoiled corn, nor even good corn, but was the daughter and granddaughter or niece of confirmed alienated pellagrins.

## CHAPTER VIII

### PATHOLOGICAL ANATOMY.

The researches of Babès, Sion and Marinesco, as well as those of the Italian investigators Rossi, Righetti, Grimaldi, made by the method of Nissl, have shown that there occurs in pellagra considerable cellular change. Parhon and Papinian noted (1905) in a case of pellagra, alterations of the neurofibrils predominating in the large cells. The giant cells show a red-mahogany coloration of their cytoplasm and a complete absence of neurofibrils. The nucleus is, according to the stage of the process, vesicular, atrophied or invisible. The nucleolus takes a stain with difficulty in the most altered cells. The appearance of the large cells of the anterior horn resemble very much the giant cells of the Rolandic area (Régis).

The pathological changes seen in 113 autopsies, seventy of which were done by Lombroso and his students, in their essential details, are given in the pages which follow.

*Meninges and Brain.*—Milky opacity of the pia mater and thickening of the pia mater and arachnoid, often circumscribed, more frequently diffuse, were found thirty-three times; four times with a purulent exudate; five times with hemorrhagic extravasations under the arachnoid; twenty-four times extensive or partial edema of the brain, sometimes with edematous softening around the pillars of the fornix or at the foot of the hippocampus; five

times hardening of the cerebellum was seen; on the other hand, in 8 cases it was found soft and edematous; eleven times atrophy of the brain, especially in the cortical substance. The weight of the brain was found diminished in 18 out of 28 cases examined, while in 7 cases it was increased above normal; twice it was found hardened; five times hyperemia of the brain was noted, twice of the corpus striatum, in one of which cases it was more marked on the right side than the left; four times, on the contrary, there was seen anemia of the brain.

Other observers have likewise noted similar changes. Nardi, Fanzago and Strambio report injection of the membranes, with thickening of the arachnoid and congestion of the sinuses. In almost all of his autopsies, Liberali found inflammatory changes in the arachnoid. In 21 out of 41 cases Verga found adhesions of the dura mater to the superior cranial bones; twice thickening of the dura mater; three times opacities of the arachnoid; and once only adhesions of the pia mater.

In 16 autopsies Rizzi found the pia mater always involved. Morelli often found extravasations of blood under the meninges. Verga found in eight cases hydrops of the ventricles, and in four softening of the cerebral substance.

Microscopic examination showed 11 times fatty or pigmentary degenerations, 4 times both combined, in the walls of the cerebral capillaries, three times with calcareous degeneration; once sclerotic changes in the brain; once dilatation of the brain capillaries. In twelve examinations of the sympathetic ganglia



Plate XVI. South Carolina case. "Wet" dermatitis of hands, face and lips. Note characteristic facial expression. Courtesy of Dr. J. J. Watson.





marked pigmentation of the ganglionic cells was found eight times.

*Spinal Meninges.*—Still more important were the alterations of the meninges found by Lombroso, Tonnini and Belmondo in 71 autopsies.

Tonnini found hemorrhage under the arachnoid 4 times in 51 cases, of which two cases were scorbutic; in other cases no hemorrhage was found, but a decided circumscribed pigmentation in certain parts of the spinal meninges. Anemia of the membranes was found in 8 cases out of 51 with concomitant anemia of the spinal cord also.

Hyperemia of the membranes was found 17 times, the arteries and veins being tortuous, and the internal face of the dura mater sometimes mottled by dark red spots. In these cases the cerebrospinal fluid was increased as well as turbid and reddish in color. In 34 out of 71 autopsies Tonnini and Belmondo found, besides the thickening of the membranes, osteomata (ossifying arachnoiditis) in addition to senile alterations. Out of 14 autopsies Tamburini found osteomata in 9 cases where the age exceeded 50 years, but all were paralytics.

*Spinal Cord.*—Omitting older writers, Liberali, Verga, Labus, Nardi, Marcè, Billod, Brunetti and Bouchard, have studied the spinal lesions in pelagra.

In an examination of the two halves of the gray axis Tonnini found in six out of fifty-one cases, granular and pigmentary degenerations with cellular atrophy. He observed changes in the left dorsal segments in one individual who had muscular atrophy

of the thorax and the inferior extremities. The amyotrophy was on the left side while on the right there were signs of anterior poliomyelitis. In this case, microscopically, there were observed cellular atrophy in the anterior horn of the left side, granulocellular degeneration on the right and incipient degenerations in both lateral columns.

In twenty-two out of fifty-three cases he found softening of the cord in the dorsal region; in fifteen, softening in the cervical region along with similar changes in the dorsal and lumbar regions. The central canal may be dilated (Syringomyelia). Eleven times out of fifty cases he found anemia of the cord, a condition more marked in the substance of the cord than in its membranes.

Microscopic examination of the cord by Golgi's method showed in places many nerve fibres poor in myelin, and demonstrated numerous round or oval nucleated bodies, thirty to sixty *micra* in diameter, many of which were surrounded by a fine stroma of granular protoplasm with proliferations.

Tonnini in eight of thirteen cases found marked pigmentation of the cells of the anterior and posterior horns with disappearance or alteration of their nuclei. From these and other lesions Tonnini thought the microscopic anatomy very similar to that found by Tuczec in ergotism.

Hieronimis noted small-cell infiltration of the gray and white substance of the cord, and around the ependyma with dilatation of the perivascular and pericellular lymph spaces. Marchi noted alterations in the vessels of the gray matter.

Belmondo, in his very important researches on twenty cases, distinguished two kinds of changes, the acute and the chronic: The first were noted exclusively in cases terminating with so-called typhoid pellagra, and consisted in an abundant infiltration by leucocytes of the meninges and of the cord, and in a great dilatation of the vessels, which were filled with blood; in other words, there existed an acute meningo-myelitis.

The alterations of a chronic nature existed, on the other hand, also in cases of severe pellagra in which death had been due to an intercurrent malady.

In all cases he found varying degrees of degeneration of the crossed pyramidal tracts, from slight changes with loss of myelin up to an actual sclerosis.

The posterior columns, those of Goll and Burdach, exhibited also degenerative changes. These lesions of the posterior cord resembled in many cases those of incipient tabes, but in the pellagrous the posterior columns were more involved in the superior dorsal and cervical regions.

Other less important changes were noted occasionally in the white substance of the cord; as well as certain alterations in the ganglionic cells, which were frequently atrophic and, even in the youngest cells, filled with pigment.

This increased pigmentation, found constantly by Lombroso in the sympathetic and spinal ganglia, is regarded by him as of much importance, being an indication of profound nutritional disturbances occurring in the central nervous system.

Belmondo, from these researches, concluded that severe cases of pellagra are accompanied constantly by systemic degenerations of the lateral and posterior columns of the spinal cord in the form of a combined sclerosis. According to Italian authorities, combined scleroses are more usual.

These cord lesions of pellagra, like those of ergotism, are not indeed essentially progressive in their nature; advance in the process is due to renewed poisoning by the toxic agent, and often it is only with the appearance of other intercurrent morbid conditions, especially a cachectic state, that the process shows any advancement; and such progress is always slow.

Since 1894, Pierre Marie has made several investigations of the alterations of the cord in pellagra; and he has undertaken to compare the cord lesions of tabes and of pellagra. He says: "Thus it is that in pellagra, where there exist most often combined lesions of the posterior and lateral columns one can, according to Tuzek's recent work, show that the degeneration in the posterior columns has a localization different from that of tabes. Indeed there does not exist in pellagra, contrary to what is found in tabes, any lesion either of the posterior roots or of their intramedullary prolongations (zone of Lissauer and Clarke's column). The degeneration of the posterior columns must then be attributed to a mechanism other than that of tabes. Indeed while the degeneration of the posterior columns in tabes is *exogenous*, that is, arises especially from the lesion

of the posterior roots; that of pellagra—at least in typical cases—is *endogenous*, that is, it takes its origin in consequence of the alteration of certain cells of the gray matter of the cord known under the name of ‘cells of the posterior columns.’ This alteration would be produced by a poliomyelitis especially marked in the upper median dorsal region, but extending almost all the length of the spinal axis. With regard to degeneration in the lateral columns, this would be due to this same poliomyelitis acting on the ‘cells of the lateral columns.’” In all probability it is necessary to consider the process in the cases of pellagrous myelitis as an intoxication in which the vessels of the gray matter play the principal role.

Dide and Leborgne have described in certain cases of non-pellagrous dementia precox, lesions identical with those noted by P. Marie in paretic pellagrins. They also found them in old epileptics. With Dide, the author presented to the Anatomical Society spinal cords of patients who died of dementia precox with analogous lesions, whereas the spinal cords of pellagrins, collected by him, in Italy at Tessin, did not present characteristic alterations. It appears, therefore, that certain insane pellagrins present cord lesions relatively independent of pellagra, which arise from secondary auto-intoxications, not characteristic of their pellagrous intoxication.

Duse<sup>1</sup> found in a great number of pellagrins a marked frequency of the Babinski reflex. Galesesco

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<sup>1</sup>Archiv. di Psichiatria, January, 1904.

and Slatinéano,<sup>1</sup> of Bucharest, have made examinations of the cerebro-spinal fluid with practically negative results, but when this is from cases of paretic pellagra or general paralysis associated with pellagra, one may conceive the possibility of a diagnostic change in the albumen of the spinal fluid, and of an increased number of lymphocytes due to a concomitant general paralysis.

*Lungs.*—The frequency of edema, pleurisy, hyperemia, emphysema, and pneumonia in the autopsies on pellagra in Lombardy is established; tuberculosis, however, seems rare there. Still at Trent in fifteen autopsies nine cases of tuberculosis were found.

*Heart.*—The examinations of the heart showed twelve times hypertrophy, sixteen times atrophy (Baruffi, Verga), thirty-three times softening of the myocardium; seven times hydropericardium; eleven times aortic atheroma. Verga found once aneurism of the aorta, and twice hypertrophy of the heart. Labus found, in one hundred autopsies, fifteen cases of hypertrophy and atrophy of the heart in advanced and old pellagrins. With the microscope very notable changes were found: most frequently brown atrophy of the muscle with cellular infiltration (twenty-eight cases in thirty-five) or fatty degeneration.

*Liver.*—The lesions of the liver are very common; it is sometimes small, again enlarged and friable, and brown atrophy occurs. Verga noted cirrheses and Chiarugi found in twenty-nine autopsies, nine fatty livers. The weight of the liver is often sensi-

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<sup>1</sup>Société de Biologie, 2 Aout, 1907.

bly diminished, sometimes by half; fatty infiltration also is found and congestion or granulo-fatty degeneration.

*Spleen.*—The spleen is also frequently atrophied, forty-one times to twelve hypertrophies. Labus and Verga likewise reported atrophy of the spleen even in cases of typhoid pellagra.

*Kidneys.*—These are often fatty, atrophied, cirrhotic or cystic (once uric acid calculus). Very rarely they appear normal. In forty out of fifty-two cases the weight of the kidneys was found diminished; almost always renal sclerosis is asymmetrical. Gianelli notes the frequency of Bright's disease in pellagra, and fatty degeneration of the epithelium of the tubules is observed with or without interstitial sclerosis (Festler).

Vassale and Belmondo have described in cases of pellagra a form of chronic nephritis with fatty degeneration and desquamation of the epithelium of the tubules.

*Intestines.*—For many years muscular atrophy has been described; also hyperemia and ulceration of the rectum, to which too much importance has been accorded. Rarely anemia or hyperemia of the gastric and intestinal mucosa have been noted (twice in seventy autopsies), as well as chronic enteritis with or without cicatricial constriction, thickening of Peyer's patches and cystic degeneration of the sub-mucuous glands.

The examination of the suprarenal capsules, of the pancreas and of the testicles offered nothing notable.



The female sexual organs, however, showed various alterations, hyperemias, polyps, tumors, fibromata of the uterus, calcarious bodies in the ovaries, etc., etc.

*Muscular System.*—In forty-four cases the muscular system was found atrophied twenty-one times; normal or well developed twenty times; athletic once; affected with fatty degeneration twice.

*Skeleton.*—Fragility of the ribs was met with in eighteen cases out of forty-two. These persons weighed from forty-nine to fifty-three kilograms, were not of an advanced age, and had, in part, craniums more solid and heavier than normal. In a single one of the cases the cranium was also fragile; in eleven the bones of the skull were thin.

Fragility of the bones was long ago observed, but without special importance being attached to it (Bouchard, Orsolato, Villergois, Strambio, the elder). This fragility depends on the eccentric atrophy of the compact substance with hypertrophy of the medullary substance, which the microscope demonstrates.

In the tubular bones, as in the spleen, numerous cells were found, in which were included red corpuscles, one part of which was well preserved, and the other part transformed into granular pigment.

*Skin.*—Griffini has made a comparative study of the alterations of the skin in pellagra with the skin of healthy subjects, young and old. He found marked atrophy of the stratum corneum, copious desquamation, active reproduction in the Malpighian reticulum and marked sclerosis of the vessels of the papillary layer and the derma.

Lombroso thus sums up the pathology of pellagra:

There are found irritations, exudations and hyperemias localized more commonly in the membranes of the brain, spleen, liver, kidneys, inferior portions of the intestines and above all in the spinal cord and its coverings.

Atrophy of many organs occurs; especially those innervated by the pneumogastric: heart, kidneys, spleen, liver, intestines and lungs; besides these, the ribs and the muscles. Brown atrophy of the heart with cellular infiltration and diminution of weight was found frequently in the absence of general marasmus and this, with other visceral atrophies, is common even in well nourished individuals. Fragility of the bones is ordinarily confined to the ribs. Fatty degeneration of the muscles is infrequent and then usually confined to certain muscle groups.

Fatty degenerations are common, and such changes are observed in the kidneys, liver and at times in the heart; and, what is of more import, in the spinal and cerebral vessels.

Very characteristic of pellagra is the great frequency of pigmentary degenerations.

Thus, as noted, one finds brown atrophy of the heart, which is an atrophy with pigmentation; pigmentation of the liver cells and sometimes pigmentation of the cerebral vessels and of the spinal and ganglionic cells, with or without fatty degeneration. In one case was seen a general pigmentation of the kidneys, the heart, the liver, and the vessels of the brain (hemolytic cellular disintegration).



There are rarely also other forms of anatomic degeneration, as calcareous degeneration of the cerebral vessels and at times aneurysmal dilatations. These alterations, together with the thickening of the membranes of the brain and of its vessels, suffice to explain the psychic troubles so frequently met with.

To be noted finally is the tendency to precocious senility, with atheroma, a great number of amylaceous bodies in the spinal cord and in the sympathetic ganglia, precocious baldness and scleroses and pigmentation of the ectodermic structures.

[Tuczek's well-known studies on the pathology of pellagra are thus summarized by himself:\*

"Putting on one side appearances incidental to the general constitutional disturbance, and those due to intercurrent disease, etc., found in pellagra—*e. g.*, general nutritional derangements which are not constantly present, such as wasting of the adipose and muscular tissues, fragilitas ossium, degeneration of the cardiac muscular tissue, fatty degeneration and atrophy with a slight degree of sclerosis of the liver, spleen and kidneys, we have to consider the more important post mortem results obtained in pellagrous patients. These are: (1) Changes in the intestinal tract—attenuation of the intestinal wall in consequence of atrophy of the muscular coat, with occasional hyperemia and ulceration of the lower

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\*Tuke, D. H.—A Dictionary of Psychological Medicine—Phila., 1892.

parts of the canal; (2) abnormal pigmentary deposit, such as is usually met with only in senility, is commonly found, especially in the ganglionic cells, the muscles of the heart, the hepatic cells and in the spleen; (3) changes in the nervous system; these are by far the most important and constant post mortem signs. The hyperemic and anemic conditions, or the edema of the central nervous system, though frequently present, are by no means the characteristic changes, neither are those inflammatory conditions such as pachymeningitis and cerebral and spinal leptomeningitis, or the obliteration of the spinal canal by granulations, or ossific arachnitis, at all peculiar to this malady, they being common to many chronic nervous affections; the most noteworthy and constant lesion, and one that may be taken as peculiar to this disorder, is an affection of the spinal cord, and especially of its lateral columns. The brain when examined furnishes generally negative results, apart from the occasionally found pigmentary deposits in the cortical cells, and in the adventitia of the smaller vessels, with fatty degeneration or calcification of the intima; atrophy of the cerebrum and its cortex has been found in cases of long standing mental derangement. The cord lesion, though mainly one of the lateral columns, frequently implicates also the posterior columns; in the former the pyramidal tracts are generally affected with partial involvement of the anterior columns; in the latter the postero-lateral columns are generally left free. The lesion of the lateral columns is shown most prominently in the



dorsal regions of the cord, while that of the posterior columns is limited to, or rather most distinctly marked in, the cervical and dorsal regions.

"Microscopically, the affection seems to be a primary degeneration of the nerve fibres, with secondary proliferation of the neuroglia, the walls of the vessels not being necessarily implicated; sometimes granular cells, and more frequently amylaceous corpuscles, are met with in the degenerated areas. Degeneration of the anterior root fibres along the anterior cornua has also been demonstrated, while there is to be found in addition a more or less considerable degree of pigment atrophy of the ganglion cells in the anterior cornua, with sclerosis of the matrix and atrophy of the nerve roots. Besides the excessive pigmentary deposit found in the peripheral ganglia, both spinal and sympathetic, there are no characteristic microscopical evidences in other parts of the nervous system.

"Typhus pellagrosus furnishes us with definite post mortem results—chronic gastro-enteritis with formation of ulcers and swelling of the mesenteric glands, and well marked changes in the central nervous system, associated with secondary affection of the kidneys, lungs, pleuræ, etc., being the main features on examination. It is to be noted that the spleen is usually involved in the general visceral atrophy, and is never enlarged."

He draws a strong analogy between pellagra and ergotism both etiologically and pathologically.

[Complete and detailed reports on the pathology of pellagra in the United States are as yet wanting.

It has, however, been shown by several writers that the pathology of the disease, in a general way, shows no essential deviation from Italian pellagra. The most detailed report has been made by Harris, who has confirmed, in their usual features, the customary skin and visceral changes. With regard to the central nervous system he has found in the brain the alterations described by Babes and Sion and confirmed by Marinesco and others. These are in the nerve cells, especially in the large chromophilic cells of the cortex, the presence of unmistakable degenerative changes. The tigroid bodies fail to stain with basic dyes, and the cell becomes swollen and vacuolated. The nuclei are frequently pushed to one side, show swollen nucleoli and will not take basic stains, the pigment is also scattered throughout the cell body. The processes of the cells often appear broken and seem swollen. The pericellular, lymph spaces are dilated, and the walls of these cavities often lined with yellow pigment. In the brain tissue, small collections of lymphoid cells are frequently encountered, and the neuroglia cells in the vicinity of the blood vessels are swollen. Harris further states:\*

"In addition to the changes mentioned, I would remark that in all of my cases the small vessels of the brain seemed unusually filled with blood, and the perivascular lymph spaces were quite uniformly dilated. There were no collections of lymphoid cells anywhere in the tissue. The nerve cells showing degenerative changes usually measured less than the normal ones, and always contained a greater or less

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\*Trans. Nat'l. Pellag. Conference 1909, p. 91.

## CHAPTER IX

### DIAGNOSIS, PROGNOSIS, PROPHYLAXIS AND TREATMENT.\*

The diagnosis of pellagra in pronounced cases—with the so-called pellagrous triad of cutaneous, gastro-intestinal and nervous phenomena—presents no difficulty, but cases are not uncommon in which the diagnosis is often involved in much doubt. Outside of the erythema, which some authorities regard as pathognomonic, there is no distinctive lesion of the disease, and the diagnosis must depend “on the lights and shadows” of the clinical picture.

Early diagnosis is a matter of much importance. Camurri has recently said: “The most important medical problem now occupying the pellagrologic field is, without doubt, that of establishing an early diagnosis. Without this, it is impossible to arrest or ameliorate the harmful effects of pellagra which seem fatally inevitable.” And, of course, such a diagnosis is all too frequently involved in doubts and difficulties. Many times, of course, the diagnosis must be of a tentative nature, and treatment begun accordingly. So far as the clinical picture is concerned, we may take into consideration the history of the case; mild mental disturbances, usually of a depressed type; gastro-intestinal disturbances, such as dyspepsia, change in appetite, thirst, diarrhea or constipation; vertigo and insomnia with headache; various paresthesias, such as burning in the mouth, esophagus and stomach, or on the hands and feet, formication, bands around the body, etc.; changes in the

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\*This Chapter is by the Translators.



**Plate XVII. South Carolina case. Same as Plate XVI. Convalescent and showing pigmentation of hands and arms. Courtesy of Dr. J. J. Watson.**





knee jerks, with usual exaggeration; pupillary phenomena, especially of a unilateral character; general malaise with muscular weakness, especially in the lower extremities; possible tender spinal points; perhaps loss in weight with a generally lowered physical, nervous and mental vigor. A tentative diagnosis made on such grounds must frequently await the appearance of more conclusive symptoms, especially the erythema.

The importance of this early diagnosis has led to a search for some positive laboratory method for recognizing the disease at an early stage, and there is not an inconsiderable literature on certain blood serum reactions, thought to be of importance in this connection. These methods include the toxicity of pellagrous serum as tested on animals, and the appearance of a "maize-precipitine" in the blood of pellagrins. Camurri in a recent discussion of this subject, with a review of his own experimental work, states that the toxicity of pellagrous serum is inconstant, and hence not to be depended upon for diagnosis. The "precipitine" test, in a general way, is made by adding a small quantity of the suspected serum to a standard infusion of corn; the mixture is placed at 37 degrees C. for a few hours, and if positive, a precipitate makes its appearance. With regard to the specificity of such a reaction, and its value in diagnosis, Camurri thinks that its only value is to show that the individual is an eater of corn, and that there has been, within a short period, some lesion of the gastro-intestinal tract. From other experimental work, he deems the urine of early

pellagra to show very constantly hypoacidity with increased chlorides; and he concludes that an individual from a section where pellagra is endemic, who shows a positive "maize-precipitine" reaction in his blood serum, and who, for a brief period of time, under a constant diet, shows a urinary hypoacidity with increased chlorides, is a pellagrin in the initial stages of the malady.

These methods, in their present state, do not appear to us of much value; and even if found of value, they are now too complex for general use, and must remain restricted to the laboratory.

Naturally inquiry is made regarding the skin lesions and their value in diagnosis. The question not infrequently arises whether the disease may be recognized without skin manifestations (*pellagra sine pellagra*), or whether cutaneous lesions alone are sufficient for the recognition of the disease. The answer to such questions is not without uncertainty. On the dermatological side we have the opinion of Merk that the skin symptoms alone suffice for a diagnosis; and that the cutaneous lesions of pellagra possess the same value in diagnosis as do those of scarlatina, measles, variola and varicella in the respective diagnosis of these diseases. Roussel expressed grave doubt as to the existence of a real *pellagra sine pellagra*, and Lombroso, as we have seen, calls certain hereditary types the only true *pellagra sine pellagra*. There seems doubt as to the existence of a pellagra without skin manifestations at some stage of the disease. Certainly such a diagnosis may be made

tentatively, but in the present state of our rather limited experience with this disease, it would seem wise for us to use great care in doubtful cases. The diagnosis of pellagra has become fashionable of late, and it has been pointed out by more than one observer that we are at present far more likely to recognize pellagra in too many patients than in too few. With riper experience we shall be able to advance with more assured step.

Typhoid pellagra and certain acute manifestations may at times be very confusing, especially in the absence of a distinct erythema. The history of such cases, and a careful search for poorly marked skin manifestations, may be of much importance in diagnosis.

In the differential diagnosis many conditions demand some consideration. In the first place, there are some diseases thought to be allied to pellagra on its etiological side, which may display some similarity in their symptomatology, such as ergotism from rye, lathyrism from chick peas and acrodynia. Ergotism is rare abroad and probably is seldom seen in this country; the history and course of the case with the spasmodic and gangrenous phenomena should serve to differentiate it. Lathyrism is lacking in skin manifestations, is usually sudden in onset, and displays a characteristic palsy. Acrodynia seems to simulate pellagra at times very closely. It is an epidemic disease, the etiology of which is doubtful, but it is thought to be similar to ergotism and pellagra. It has been observed in France, Belgium, Turkey, Persia, Algiers and Mexico, always in epidemic

form. There are gastro-intestinal symptoms, hyperesthesias, anesthetics, edemas, and an erythema, principally confined to hands and feet. Spastic phenomena sometimes occur. The course is afebrile and recovery is the rule. Fatalities are rare.

Scurvy, leprosy and beri-beri are often mentioned but should be easily recognized.

Various skin lesions, such as solar erythema, lichen, eczema and erythema multiforme may be important. Erythema multiforme may at times be a real cause of confusion. Its recognition must depend on its characteristic cutaneous lesions, the course of the disease and the general symptomatology. A solar erythema may for a time cause doubt, especially when occurring among the insane. Lichen and eczema must be excluded on local appearances and general course.

Functional neuroses, especially neurasthenic phenomena, may for a time remain in doubt, but they are usually cleared up by the appearance of the erythema.

Sprue is said to occur in the United States and may cause confusion; the course of the disease and the absence of skin manifestations must suffice for diagnosis.

Typhoid pellagra may be mistaken for an acute infectious disease or uremia or diabetic coma. The history of the case under such circumstances may be of much importance. The character of the temperature, condition of internal organs and general symptomatology should usually serve for differentiation after a short time of observation.

## PROGNOSIS.

There are two factors, with regard to pellagra in the United States, which should not be overlooked in dealing with prognosis. These are, first our comparatively brief experience with the disease; and, second, the fact that even this experience is based very largely on the treatment of asylum cases, admittedly the most hopeless type of the disease. It is manifestly unfair to expect improvement from any treatment when it is applied to cases not only far advanced, but likewise victims perhaps of many serious secondary organic changes.

Nevertheless, even when these factors are given due consideration, it may undoubtedly be safely said that in this country all physicians who have treated this disease regard the outlook in individual cases as one of great gravity with respect to complete and final recovery. The statistics in existence, all based on asylum cases and only a small number at that, will give a case mortality of from 35 per cent. to 65 per cent. Such figures should really not be quoted, for they certainly give a very erroneous estimate as to the gravity of the disease in this country, and justify no definite conclusions whatever. In the existing state of our knowledge definite information is not available, and the opinions of those with widest experience must be accepted as our only present criterion. This opinion is practically unanimous that the prognosis is grave in all cases.

Allbutt has said, "When the disease has recurred for three or four seasons, and especially if the mind be affected, the prognosis is very bad. I gathered

from the physicians of Italian lunatic asylums that recovery of patients once arrived at the asylum stage of insanity is almost unknown. Still these are extreme cases; the mentally afflicted in their earlier phases may recover; only too often, however, the advance of death is inexorable," and this doubtless expresses very fairly the view generally entertained in this country at the present time.

A study of Italian statistics, however, certainly leaves one to infer that the Italians have no such mortality as we have apparently had; and it is probably safe to assert that the average Italian case mortality, as given in their statistics, will not exceed that usually accepted for typhoid fever, that is 10 per cent. In many cases it will fall even lower than this. The nature of the disease, however, with its chronic course and seasonal recrudescences, and the notorious unreliability of many statistics on pellagra, leaves the matter in much doubt. At the same time it would certainly seem that the Italian physicians do not view the matter in the hopeless light that is common among so many American medical men. The Roumanian observers, who with the Italians have perhaps the widest experience, likewise do not take this gloomy view with regard to prognosis.

From a consideration of all these facts, we are forced to conclude either that the disease is much more severe and hopeless with us; or, what is far more likely, that our experience has been largely confined to the hopeless type of the disease, the asylum cases. It seems to us reasonable to think that as our knowledge broadens and our experience

develops we will probably come to a clearer comprehension of the matter; and we will finally, in all likelihood, conclude that while the prognosis in all cases is grave, it is by no means hopeless.

There are certain considerations of much weight in prognosis, and among these one of the more important is an early diagnosis. It seems to be a fairly unanimous opinion, throughout pellagra literature, that early cases offer the greatest returns from treatment, and, of course, the most hopeful prognosis. The disease is essentially chronic in its character, but, untreated, advances inexorably until finally with marked involvement of the central nervous system little can be hoped for from treatment.

It does not seem unjust to draw some parallel between this disease and tubercle of the lungs, both chronic, advancing states. But we have, through much misery and suffering, learned how early to diagnose, to treat and to counsel the tuberculous. Can we not apply this lesson, at least to some extent, with regard to pellagra? Pellagra is subject to sudden acute manifestations, and these conditions are of the utmost gravity. The condition of typhoid pellagra is practically hopeless. Occasionally a case recovers, but this is very rare. The chronic type of the disease, without mental involvement, is, as a rule, the most hopeful type, especially if early treatment is begun.

Certain symptoms are worthy of note with regard to prognosis. As a rule pellagra is a disease of little fever, and it is fairly generally acknowledged that fever, especially if high or constant, must be



regarded as a danger signal. (See p. 214.) The character and extent of the erythema, since the time of Strambio, has been regarded as no index of the constitutional disturbance, but we are convinced that extensive, moist dermatitis is always accompanied by grave general conditions. This opinion has likewise been expressed by Merk in his recent admirable study of the skin lesions. Whether such erythemas mean some secondary invasion we are not in a position just now to say. Mental involvement always adds to the seriousness of the outlook, and such nervous disturbances as subsultus, marked tremor, retraction of the head, can, as in other affections, be interpreted as an index of severe intoxication. In mental cases periods of excitement are not rare and they do much to help exhaust the patient. Severe recrudescences of the acute phenomena sometimes occur during the same season after the patient seemed to be on the road to recovery. Steadily progressing emaciation, especially if accompanied by an inveterate diarrhea, which is usual, very often ends fatally. On the contrary, a tendency to take on fat is usually a favorable sign.

Much of this might be summed up in a general way by saying that in advanced cases, with serious involvement of the central nervous system, and the appearance of what Roussel calls various consecutive conditions, offer a far less hopeful prognosis than cases of the first or early second stage before such events have occurred.

Certain complications are also of importance in prognosis, and should always be kept in mind. By

some malaria is regarded as a very serious complication. Then we may have intestinal parasites, such as thread worms, round worms, hookworms and amebas. Marked nephritis may also occur as well as acute bronchitis, pneumonias, decubitus gangrene (often difficult to avoid), possibly tubercle, and, of course, sudden acute manifestations like typhoid pellagra. All these complications may add greatly to the gravity of the situation.

Finally, if the patient is carried safely through the acute manifestations of one season, a recrudescence of them must be watched for during the next season, more especially if anything should intervene to lower the general resistance, such as acute illness, childbirth, etc. Being a chronic disease, pellagra demands long, continued oversight and treatment much the same as does syphilis.

It may be added that an hereditary taint may prove of much importance in prognosis, as has already been pointed out elsewhere.

#### PROPHYLAXIS.

In any discussion of pellagra we must of course recognize the paramount importance of prophylaxis. The disease is first of all a public health problem; and while the treatment of the individual case must necessarily appeal to many medical men, yet preventive measures should, and do, occupy first place. Governments have usually displayed much concern at the invasion of their territory by this disease, and medical men, sanitarians and legislators have joined hands in attempts at its limitation or eradication.

The gravity with which the disease is regarded, both in the individual case and in its relation to pub-

lic health, becomes much more evident when certain facts are brought into prominence. Pellagra has almost invariably been found associated with wretchedness and poverty, and the disease has in consequence been often regarded as an indication of the economic conditions obtaining among certain classes of people in the country involved; and thus through motives of patriotism or for reasons of policy, or even from a sense of shame, publicists have felt urged to grapple with the problem. Pellagra, moreover, largely involves the laboring classes and so menaces the physical integrity of a very important part of a nation's population, a part which usually forms an essential element of strength and productivity. Through its hereditary influences the disease also saps the strength of the people in a peculiarly hopeless manner, and throws its burden upon coming generations, ever spreading wider in its vicious circle. Furthermore, the chronic nature of the disease, its seasonal recurrences, its too often steady advance, with possible years of invalidism and not infrequent mental alienation—all result, not only in the loss of productive years to the nation, but likewise often to the assumption of the greater burden of caring for useless members of society, frequently at public expense in a public institution, for long periods of time. These, in a general way, are the peculiar reasons why pellagra is regarded as a public health question of no small importance; and why this disease, less important numerically than some other well-known, preventable diseases, has yet frequently attracted the at-

tention of sanitarians and public health officials, and demanded the support of legislators in the enactment of laws and in the appropriation of money.

Now, the prophylaxis of any disease must necessarily depend upon its cause, and with equal necessity the efficiency of prophylactic measures must be in ratio to the definiteness of our knowledge regarding such cause. The etiological ideas of pellagra from a scientific viewpoint are, it may be admitted, at least in an unsatisfactory state. Yet, despite this, men of the widest experience and the broadest study seem convinced that there is some definite etiological relation between pellagra and the use of spoiled corn as a food stuff. On this assumption they have established extensive prophylactic measures which apparently in great part have often met with success. Under present conditions we must, it would seem, try to profit by their example. Of all such work, perhaps none deserves more attention or study from us than that of the Italians. They have labored long and earnestly in this matter, and they are beginning to believe that their success is almost assured.

There is one fact, however, of immense importance in the United States which must not be overlooked, and which has been commented on by many observers, and that is the absence among us, relatively speaking, of the poverty-stricken classes among which pellagra occurs. It has been said that Americans do not know what poverty is, and certainly we have no such wretchedness and poverty in our country as is found in many places in the old world. This fact adds a hopeful gleam to an otherwise dark out-

look, and it may not be too much to say that for this reason alone pellagra will never secure the hold here which it has in other places. But we could hardly sit with folded hands depending upon this fact for the solution of so serious a matter. We must at least be awake to the possibilities which may lie in the appearance among us of a disease of such character as pellagra.

As for the methods adopted by the Italians and the results, so far of their struggle, no better idea could be given than in a brief review of some portions of the report of Mr. Cutting, elsewhere cited in this volume. He personally visited many districts in Italy and saw not only the men engaged in the fight against pellagra, but was able in many places to judge also of local conditions for himself.

He says: "How shall the people be prevented from eating mouldy corn? This is the problem which confronts the legislator and philanthropist of today. For its clear realization and for the chief measures adopted to solve it, we are indebted to the Zeist School, and in particular to Lombroso. \* \* \*

The Zeists have compelled general recognition of the obvious truth that prevention is better than cure; and at the same time, by the very dogmatism of their monistic creed, have given unity of object to the work of prevention." He then reviews Italy's early efforts against pellagra, notes the establishment by Joseph II of Austria in 1784 of a special hospital for the study of the disease at Legnano with Gaetano Strambio as director; and the important census of pellagrous sufferers made by national authority in

1879, the consequences of which were renewed interest in the disease and much activity on the part of various provincial governments against its further spread. The way was thus finally smoothed for the great national law of 1902, under which the present apparently successful struggle is being waged against this disease. (This law and the regulations made under it are given in Appendices I and II.)

The important dispositions of this act, according to Cutting's analysis, are of two kinds, curative and preventive; the former include distribution of salt, administration of food, either at the patient's homes or at sanitary stations (*locande sanitarie*), treatment of severe cases in hospitals, pellagrous hospitals (*pellagrosari*) and insane asylums. The preventive measures include the inspection and testing of all corn or meal brought in at the frontiers or seaports or offered for sale or brought to the mills; the exchange of good corn for bad; dessicating plants, cheap co-operative kitchens; improvement of agricultural methods; and the education of the people as to the danger of bad corn. In addition, cases of pellagra must be reported.

There are some practical methods authorized by the bill and in general use in Italy which deserve a brief discussion, since they are in a measure novel to us in the United States, and are deemed of much importance.

The free distribution of salt is due to the fact that salt is a government monopoly in Italy and its price is frequently high. Besides being considered an essential part of a healthy diet, salt is also by many

considered beneficial to pellagrous sufferers. It is stated that the national government in Italy distributed over 3,000,000 pounds of salt in this way during 1906-07.

Under the law of 1902 the distribution of a "curative diet" is made obligatory, and it is provided that such diet shall be distributed for two periods of at least forty days each per annum. This diet is approved by the provincial Pellagrologic Commission, and medicines are also included.

These provisions are carried out by means of a house to house distribution, by economic kitchens, or by sanitary stations, all dependent upon the practical conditions to be met in various places.

The economic kitchen is a place where good, plain food is supplied to rural populations at a low cost, or even gratuitously. Such places are conducted by the commune or by charitable organizations or they are co-operative.

The sanitary station (*locanda sanitaria*) is a development of the economic kitchen in accordance with special conditions, and is a place where pellagrins come once or twice a day, during a stated period, to receive food which is consumed at the station. The food consists of soup, bread, meat, wine, cheese, milk and vegetables. The general idea is to furnish good nutritious, non-maidic food to pellagrous sufferers during the seasons when pellagra is most virulent, spring and fall. Along with the diet, in many such stations a course of medical treatment including hydrotherapy, is given as well.

The value of these stations, according to Cutting, is a subject of much discussion. The time of treatment is too brief, but a large number of sufferers are reached, and more than 80 per cent. go away distinctly improved, while a large number of incipient cases, especially among the young, are permanently arrested. For incipient cases it is regarded as a valuable curative agent in the fight against pellagra. In 1907 there were over five hundred of such stations in Italy. The best results are obtained where the sanitary stations are numerous and are kept open for considerable periods of time.

The *pellagrosari* are special hospitals for the treatment of pellagrins. They are intended primarily for cases too acute, or too grave, for treatment at sanitary stations. The treatment in these institutions is along the same general lines as elsewhere, dietetic, hydrotherapeutic and medicinal. There seems a tendency to make use of these institutions as a prophylactic measure, admitting thereto principally the young and the incipient cases.

The insane asylums receive a large number of alienated pellagrins, and the tendency is to send as many of these unfortunates as possible into the asylums, rather than allow them to linger in the villages and rural districts.

The inspection of corn and the prohibition of the spoiled grain is conducted by a corps of men acting under the sanitary authorities. The distinction between sound and spoiled corn is not always easy, and several tests are in use. Such tests include the general physical characteristics of the grain, dis-



coloration, presence of moulds, loss of lustre, bitter taste and peculiar odor. The chemical tests include the determination of the proportion of ash, sound corn being said not to give more than 4 per cent. of ash; Gosio's phenolic reaction, a greenish or purple color with ferric chloride; the reaction of the grain, spoiled corn having a higher degree of acidity; the germination test, spoiled corn of course losing a certain part of its germinating power; and finally the use of animals. These tests are not regarded as entirely satisfactory, but in practice the sound and spoiled grain are said to be differentiated with a fair degree of readiness, especially at the frontiers and seaports. But meal from home-grown grain, at the mills, or on the markets, has given much trouble; and the detection of a spoiled article is said to be almost impossible. It has even been urged by many that all mills be placed under governmental supervision, or be owned and operated by the municipalities.

"Every province of Italy," says Cutting, "has a commission for the encouragement of improved methods of agriculture." Thus are established the *Cattedre Ambulanti* (moving chairs) or "Farmers' Institutes," the activity of which is far-reaching, and the influence of which has been notable in the progress of agriculture in Italy during the past decade. By precept and example these "institutes" have taught the peasant how to grow better corn, or to replace this crop with some other more profitable one, as potatoes, millet, etc. Cutting thinks it no small triumph for these institutions that in many



**Plate XVIII. South Carolina case. "Wet" form. Dermatitis of hands, elbows, face and lips. Superficial ulceration of hands.**



places they have induced the Italian peasant to abandon a traditional crop for one unfamiliar to him. The influence of such work is thought to be one of the important factors in the restriction of pellagra.

The dessicating plants for the artificial drying of corn are of comparatively recent introduction into Italy, but are regarded as of the greatest importance in the prophylaxis of pellagra. The peasantry not infrequently object to the use of the dessicator, alleging that during the process the corn loses in weight, later it will not germinate and that the cost amounts to something. These objections do not all hold good, for the loss in weight from the spoiling of the grain is also considerable, the best dessicators do not impair the germinating power of the grain, and the question of cost has been met by a provision of the law which allows dessication of corn for family consumption at no cost, and the rest at nominal rates.

These dessicators are of two types, fixed and portable. The portable are very convenient, but the fixed are far more efficient and are preferable.

Cutting, in describing the Cattaneo type of the fixed dessicator, says: "Air heated by a furnace is forced by a ventilator into a chamber of seven stories. Each story is a circular, revolving tray, containing about 1,390 pounds of corn. The top tray is filled from above. After a certain time its contents are emptied, by pressing a lever, into the tray below, in such a way that they are thoroughly remixed. The corn thus passes gradually to the

bottom tray, whence it goes to a receptacle where it is cooled by means of a ventilator, and thence out of the machine by an inclined plane. The first tray load of corn takes seven hours to pass through the machine; after that 1,400 pounds come out each hour. The cost of the machine is about \$540, and the power required to run it about  $2\frac{1}{2}$  H. P. . . . The air is forced through the trays in both an upward and a downward direction, and that which has absorbed dampness from the corn is replaced constantly by dry air; the temperature is kept low (about  $104^{\circ}$  F.), with economy of fuel and without risk of injuring the corn. The mechanism is so simple that the machine can be handled by any laborer of ordinary intelligence."

There are also good portable dessicators which are less elaborate and less costly, but, as stated, far less satisfactory.

The low temperature at which the grain is dried does not suffice to kill mould spores, and it is, therefore, considered of much importance not to place spoiled corn in the dessicators. Their use is to dry good grain for preservation.

Public dessicators are now numerous in Italy, the number in 1907 being given as 461, and the quantity of corn dried by them during that year as 54,747,000 pounds.

The necessity of properly storing corn, and the unhygienic and unsanitary methods in use among the peasants for preserving the grain, have been the subject of much comment. In recognition of the importance of this matter, the law of 1902 provides



for public store houses, but for the present the cost of construction and maintenance has been prohibitory. Cutting thinks there is no doubt, however, that public store houses will ultimately come into general use.

In the further effort to eliminate from the diet of the peasants bread made of corn, there has been established another institution known as the rural bakery (*forno rurale*). In this institution good wheat bread is furnished at a very low price. Institutions of this kind are comparatively recent, but their number has increased from 77 in 1904 to 591 in 1907.

Another effort has been made in the establishment of corn exchanges where the peasant may exchange spoiled grain for a smaller quantity of good meal, some deduction being made for cost of milling, etc. The plan is approved by many as a good one, and has not proven very costly in comparison with the benefit conferred, but it has not been very successful.

Numerous other expedients of less importance have been suggested or even adopted in the struggle against pellagra. "In general," says Cutting, "the object is to get at the children; to prevent pellagrous mothers from nursing their babies, or if this cannot be done, to see that the mothers are well fed; to treat a child the moment he or she shows the slightest symptoms of pellagra, and to send such children to other surroundings."

Of course while legislative restrictions have their importance, yet in this, as indeed in all such struggles, the education of the people is of paramount im-

portance. The restriction of corn, the change in a national taste, the introduction of a varied diet and better living conditions, these are the cardinal things in such a campaign. "And this is not neglected. The indefatigable Permanent Committee of the Interprovincial League against Pellagra edit a magazine, the *Revista Pellagologica Italiana*, devoted to the struggle against the disease; popular pamphlets are distributed in great numbers; popular lectures are held everywhere; colored lithographs representing the healthy laborer fed on sound corn and the pellagrous laborer fed on spoiled corn hang on the walls of public lecture halls; and the pellagologic and agricultural commissions of the different provinces multiply instructions by precept and example." (Cutting.)

The results of such work seem on the whole very encouraging, but their interpretation is difficult by reason of other contemporaneous developments. They coincide with a marked rise in general prosperity. The laborers and peasants can now eat better food than ever before; numbers of the rural population are employed in industrial institutions, where they receive a varied diet; temporary emigration has reflexly widened the view of the peasant class, and they demand and get better food and living conditions; the consumption of meat is increasing, and wages are higher. Such things must, of course, in a disease like pellagra, have a very profound effect.

Statistics undoubtedly show a decrease in pellagra; but for many reasons statistics are not

entirely satisfactory and do not serve to show the actual state of the case. The opinions of those actively engaged in the work and in close touch with the situation, are, in general, that pellagra in Italy is notably decreasing both in numbers and in intensity. Strange as it may seem, however, the disease is apparently increasing its area, and parts of Italy previously free from pellagra are now developing the disease. The cause of this is not apparent.

*Communicability.* The question of the contagiousness of pellagra, early in its history, aroused much discussion. The idea of contagion was advocated by many able men, and opposed just as strongly by others. With the courage of conviction and with the zeal of enthusiasts, several voluntarily submitted themselves to inoculation with pellagrous material in order to prove their contention of its non-contagiousness. The inability of those favoring contagion to bring forward any satisfactory reasons or observations to sustain their view, and the numerous observations and the extended experience of others against the idea of contagion, at last served entirely to discredit any doctrine of communicability; and the advocates of contagion abandoned their views. Since then this subject seems to have received but scant attention at the hands of writers on pellagra, the question being regarded as definitely settled. Roussel, as early as the middle of the nineteenth century, wrote: "It can be said of the contagion of pellagra, that it is a question fully determined, . . . pellagra is not contagious."



they do not cure, they at least prolong existence or render it more tolerable. In some patients, however, there is a true aversion to baths, and in such they should not be tried.

Of drugs in a general way he condemns the use of iron, for the reason that he has seldom seen benefit from its use and has often seen it cause exacerbations of intestinal and other symptoms. In some cases, especially in the young and those with arrested development, he states that he has obtained magnificent results with simple salt rubs or frictions. He has experimented extensively with acetate of lead, but finds it of little use except in pellagra of the aged, in those who suffer acute articular pain, in cases of incipient paresis, and in cases of general tremor. The dose used was 0.01 to 0.05 gram in 300 c. c. of water. In typhoid pellagra he tried numerous remedies without avail.

Finally in his search for a remedy (through some reports of Coletti and Perugini) he got the idea of using arsenic, and he says, after experience with the drug, that the results exceeded by far his expectations. He does not seem to regard arsenic as a true specific for pellagra and admits that it does not cure all cases, but he thinks it is a very valuable remedy, and that it acts in a certain sense as an antidote for the toxins of spoiled maize. As an antidote he compares it to the action of opium in alcoholism and mercury and the iodides in syphilis. Sodium chloride he seems to think has probably an equally powerful effect, but a very much more restricted field, being limited largely to children.

He uses arsenic in the form of Fowler's solution in dosage of 5, 10, 15, 20, and 30 drops, or in the form of pure arsenous acid (arsenic trioxide) dissolved in slightly alcoholized water, in doses of one-fortieth to one-twentieth milligram, increasing, according to tolerance, up to 0.001, 0.002, or 0.003 gram and very rarely even to 0.01 gram. The administration of the drug is suspended for a few days from time to time. He cautions against certain dangers in its use, however, and mentions as dangerous symptoms the appearance around the neck of an herpetic eruption, profuse salivation, anorexia, vomiting, diarrhea, palpitation of the heart, syncope, burning in the pharynx and stomach, headache, great muscular weakness, and bronchitis. The possibility of arsenical neuritis should be kept in mind.

He thinks certain types are especially helped by the administration of arsenic, and that certain others receive no benefit, as follows:

*Benefited.*—Cases with marked marasmus; cases with incipient paresis; cases with sitophobia (gastralgic type); cases with vague mania but not systematized delirium; cases in the aged, if not at the verge of decrepitude.

*Not benefited.*—Cases in the young and in infants; cases well nourished and robust; cases with systematized delirium; cases with mental alienation of twenty to thirty years' duration; cases having lobar pneumonia, tuberculosis, albuminuria, or severe vertigo.

In cases of grave vertigo he sometimes uses the tincture of *cocculus orientalis* in doses of 3 to 5 drops daily, progressing slowly to 30 drops a day.

Among symptomatic remedies he seems to approve the use of calomel, castor oil, bismuth subnitrate, opium, tannin and other astringents, at times chlorate of potash and astringent enemas in the treatment of the diarrhea. In certain advanced cases ergot, strychnine and faradism have sometimes been employed as useful adjuvants, and in alienated cases such hypnotics as chloral, paraldehyde and sometimes opium.

In defending his use of arsenic and salt he contends that on empirical grounds alone he can be justified, since experience has amply proven these remedies to be of immense benefit. But he furthermore states that their use can be justified on rational grounds as well, and he quotes extensive experimental work to show the beneficial effects of arsenic on the heart, skin and nervous system, its antifermentative power, its effect on metabolism, etc.; for chloride of sodium he brings forward similar evidence to show its action on the skin, its power of aiding in the assimilation of phosphates, increasing muscular force, aiding digestion, stimulating the development of cartilaginous and other tissues, its beneficial effect on the nervous system, etc.

The general measures adopted in the treatment of the disease should be dietetic, hydrotherapeutic and medicinal.

The diet is a matter of much importance and should be selected with some care. It should be easily assimilable, highly nutritious and should include meats. An abundant diet is recommended in spite of the frequent intestinal disturbances and

diarrhea. These disturbances are perhaps trophic largely, and not inflammatory, in their nature; and food is not so much contra-indicated as in some other intestinal states. Of course if the diarrhea is too free and the stools contain undigested material the diet must be regulated accordingly. It must not be forgotten, however, that the patient's condition usually requires all possible nourishments and effort must not be spared in the individual case, where possible, to meet the dietetic indications. Of course in the treatment of a number of pellagrins, as in institutions, the question of expense or feasibility often intervenes. The general diet given adults, for example, in the *locanda sanitaria* at Bagnolo Mella, in Italy, is as follows: First meal: meat broth, and coffee and milk, each on alternate days, with 150 grams of bread. Second meal: one liter of soup made of macaroni, 100 grams, vegetables, 100 grams, meat stock and condiments; boiled meat, 200 grams, with vegetables, 50 grams; bread 300 grams; wine 200 grams. Third meal:  $\frac{1}{2}$  liter of soup, made of rice, 50 grams, vegetables, 50 grams, meat stock and condiments; meat stew, 100 grams, with vegetables, 50 grams; bread 150 grams; wine 200 grams. This diet is modified in many ways to suit individual cases and appetites, and for children under twelve years is reduced in quantity.

In commenting on this diet Ceresoli, the medical director, states that digestibility, which is to a large extent dependent upon cooking, is a matter of great importance; and for this reason he commends roasted meats, which for local reasons he has not

used in his diet. Where there is repugnance to meat he substitutes cheese or eggs, and cheese he recommends highly. The wine, which is of good quality, stimulates a torpid digestion. Care is always taken by him that dietetic rules are subordinated to age, sex, temporary physiological accidents, idiosyncrasies, the condition of the gastro-enteric tract and to the greater or less tolerance of a reconstructive food supply. He also points out the especial need for nitrogenous substances in a diet for pellagrins. He seems to think it no easy matter nicely to adjust a diet to the needs of these sufferers, and that a diet, begun cautiously, can be gradually and judiciously enlarged properly to meet their needs.

Hydrotherapy is considered a valuable adjuvant in the treatment of pellagra and is extensively employed. Cold baths and warm baths, both simple and medicated, as well as douching, are employed.

Such treatment must be used with discretion, of course, and consideration given to the stage of the malady, predominating symptoms, therapeutic indications, age, sex, and general physical characteristics. In weak and prostrated individuals treatment is begun with warm baths of short duration, and the temperature is reduced and the time prolonged as the patient improves. At the extremes of life the warm bath is preferable.

The application of baths should be so regulated, of course, as to produce the best results, with increased oxidation of the tissues, more rapid elimination, greater metabolic activity, increased appetite,

improved digestion and assimilation, and a strong tonic effect on the whole organism. Improvement is evident from increase in weight, in the firmness and force of the musculature, disappearance of prostration and subjective nervous symptoms, with increased physical and moral vigor.

Vertigo, stuporous states, distressing paresthesias and even diarrhea are often benefited. Massage may sometimes be added with advantage.

The medicated baths of sulphur or arsenic are used chiefly in certain conditions of the skin, sometimes in cases with predominating intestinal disturbance accompanied by wasting.

The salt bath or rub is of especial importance in children. This may be given as follows: The child is placed in a tub of warm water, the temperature of which may be practically judged by the hand, which should be able to bear it with comfort. A convenient receptacle of salt is placed near. The salt should be of a fine quality and should not contain coarse particles. A good kitchen or cooking salt answers all requirements. The attendant, having stood the child up in the tub, wets his hands and dips up a handful of the salt. With this he thoroughly and firmly, but not roughly, rubs the child's body all over for some fifteen or twenty minutes. The child is then made to lie down in the water, the salt is washed off, and after a few minutes a cold douche is given. The child is then put to bed and at rest for a time. This may be done three or more times weekly.

For further details concerning hydrotherapy the reader must consult special works on the subject.

Among general measures rest is a matter of much importance, especially in acute conditions, and when there is fever. Change of climate and surroundings, if possible, particularly to colder latitudes, may be advised. Saline infusions may at times be of service. During the warm season avoidance of the sun's direct rays may prevent a bad erythema. Cleanliness, good nursing and fresh air are, of course, to be desired.

With regard to the medical treatment, symptomatic remedies must be used as needed. For insomnia chloral hydrate, paraldehyde, or some of the more recent hypnotics, like trional, sulfonal or veronal, may be tried. The dermatitis, if dry, may not require much attention, but moist dermatitis, especially if extensive, cause much inconvenience. Such surfaces often become infected and may prove of no small concern. Oily applications or tincture of iodine may be used on dry surfaces. The moist conditions should be treated on general surgical principles. We have found a picric acid dressing (1 per cent. aqueous solution) of benefit, but it stains linen badly. A stubborn diarrhea will give much trouble at times and may prove rebellious to all treatment; the bismuth salts, the salicylate especially, various astringents, sometimes enemas of cold water, and at times opium along with the general and dietetic management, must be depended on for its control. Pain may at times require morphine, but we have not been forced to resort to its use to any great

extent, and it is, of course, to be avoided if possible.

Complications, such as malaria, syphilis, intestinal parasites, should receive prompt attention with appropriate remedies. If much anemia be present many good observers think a bland preparation of iron is needed; some good preparation of arsenate of iron would seem of value, and such a preparation can now be obtained even for hypodermatic use. Mercury, except in cases complicated with syphilis, seems valueless. Following Wright's work with the succinamide of mercury in tuberculosis, we have given this salt a trial in several cases, but achieved no results except in syphilitic cases. The remedy proved quite irritating locally.

The more or less recent introduction of certain new arsenical compounds seemed, in the light of Lombroso's work, to offer a better therapy for pellagra. Of these preparations three have come into more or less general use. These go by the names of atoxyl, soamin and arsacetin. Atoxyl and soamin are both trade names and are stated to be forms of sodium arsanilate, containing respectively about 26 per cent. and 22 per cent. of arsenic. They are sold in the form of the salt itself or in the form of hypodermic tablets. Arsacetin, introduced by Ehrlich as an improvement over the other two, is described as an acetyl derivative of atoxyl. This is sold in the form of the salt itself.

The arsenic of these salts is said to be liberated very slowly in the system, thus producing the ordinary therapeutic effects of arsenic with the advantage of a more continuous and less toxic action and less



irritation. Toxic effects from excessive dosage have been frequently noted, although their toxicity is far less than that of arsenic trioxide. Blindness, due to degeneration of the optic nerve, has occasionally resulted.

All of these salts are soluble in water, arsacetin more so than the others, and they are largely used by the hypodermic or intramuscular method, their administration by mouth not being recommended for the reason that toxic symptoms may result from decomposition by the acids of the stomach.

There has been much discussion as to the dosage of these remedies, but based on the extensive use of atoxyl and soamin in syphilis and trypanosomiasis, it would seem efficient and safe to give as much as 0.5 to 0.65 gram on each of two succeeding days, and to repeat this dosage, with ten-day intervals, for many months. Others have given as much as 0.5 gram on alternate days until 7 grams have been given, then a rest for three months. The dosage of arsacetin is stated to be lower, but many workers have used the same dosage as with the other salts, without toxic results. Arsacetin has the advantage of being more soluble, is said to be less toxic, its solutions can be boiled and they keep well. It is perhaps needless to add that in administering these remedies antiseptic precautions should be observed, and local irritation thus avoided.

Babes, in Roumania, seems first to have used atoxyl in pellagra and reported very favorably on his results. Warnock, in Egypt, then tried it extensively, and concluded ultimately that "the value



Plate XIX. South Carolina case. "Wet" form. Lesions identical with those of Plate XVIII. Both cases under observation at same time and both rapidly fatal.



of atoxyl in the treatment of advanced stages of pellagra such as are met with in this asylum has not been demonstrated," and he could not confirm the Roumanian experience.

Reports on the use of these remedies in the United States have been almost universally unfavorable. We have used both soamin and atoxyl rather extensively, but have had only a limited experience with arsacetin. We have used them almost exclusively by the intramuscular method, and have observed no toxic effects except in one case. Our usual dosage has been 0.5 to 0.65 gram on alternate days for two to three doses, then a rest of ten days, and repeat for several weeks. Our work has largely been done with asylum cases, and the results have been disappointing. With a few non-asylum cases, however, we have noted improvement; and we are not inclined, as yet, to discard these remedies as useless. Inveterate diarrheas have seemed at times to yield to atoxyl or soamin.

Recently Babes, and others, have reported brilliant results from the use of atoxyl and arsenic trioxide combined. The method is as follows: Atoxyl 0.5 gram hypodermatically; externally on the sound skin, a rub with 5. grams of an ointment of arsenic trioxide (1 to 50); and internally a pill of arsenic trioxide (.001 to .002 gram) thrice daily; this treatment is given on two successive days, and, if necessary, is repeated once after an interval of one week. We have given this method a limited trial, but without observed benefit.

We have used Fowler's solution of arsenic in many cases with apparently good effect. Donovan's solution has likewise been employed by some. It is needless to add that scores of other remedies have been employed and recommended in the treatment of pellagra, but they have not borne the test of time.

Finally, we have the serum treatment and blood transfusion. There is a good deal of evidence tending to show that specific antibodies are developed in the blood of pellagrins, and the serum of recovered cases has been reported as successfully used in the treatment of typhoid pellagra. Some workers have even expressed the confident hope of producing from the horse an efficient antiserum, but this has not yet been realized. It has also been suggested that possibly so-called "blind staggers" in horses may be pellagra, and that the serum of animals recovered from this disease may be efficient in treatment.

We have attempted to treat two cases with blood serum taken from recovered pellagrins. One case died from a pneumonia shortly after treatment was begun, the other seemed to improve for a while, but finally, after much emaciation, died of an intercurrent tubercle of the lungs. It is difficult to secure proper cured cases, otherwise such treatment is not difficult to carry out, and would seem well worth further effort.

Cole has treated a number of cases by blood transfusion, after Crile's method, and reports very good results. For donors he has used both recovered pellagrins and others who have not had the disease. This procedure, while not difficult, requires expe-

rience. It is more difficult of application among the insane by reason of lack of coöperation on the part of the patient. Under certain conditions it may be regarded as a valuable surgical resource.

The benefits of a change of climate were long ago recognized by the Italians and French and recently have been recommended in this country by Bass and others.

In conclusion, it may be said that treatment of advanced stages of the disease, especially in asylums, is very unsatisfactory. Early cases, without mental involvement, however, can be often successfully reached. Furthermore, in a disease like pellagra where so many persons are involved, especially among the poorer classes, the great desideratum is, of course, some specific treatment, inexpensive and easy to use. Elaborate and expensive measures do not fulfil the indications; and while such resources are of great value under certain rather exceptional conditions, they are, for general use, largely inappropriate.

## CHAPTER X

### CORN AND PELLAGRA IN FRANCE. ROUSSEL AND LOMBROSO.

It would seem evident from what has been said that the prime necessity in the prophylaxis of pellagra would be a radical change in dietary, but the practical question at once arises as to the means to be adopted in carrying out this reform; and the further difficulty as to whether corn, even if sound, should be interdicted. This immediately suggests an inquiry as to the food value or danger of corn of good quality.

#### FOOD VALUE OF CORN.

Not a few have asserted that pellagra may be due to a scarcity of nitrogenous material in corn, a scarcity all the more pernicious for that class of people like the peasants (in whom all admit a greater frequency of pellagra) who must constantly do severe manual labor.

An attempt has been made to justify such an hypothesis from the less intensity of the disease among those who eat meat, like the city dwellers or the rich; and from the preference which is even yet given by the physiologists to nitrogenous food over a vegetable diet; such considerations stimulating the belief that a lack of meat is dangerous to human health.

Lombroso has shown how almost all the laboring classes and peasants of Europe live upon a vegetable diet; and likewise the laboring populations of other nations as, for example, the Chinese and Japanese.

As Beketoff\* has said: "The physiologists have exaggerated certain statements on dietetics. They have not taken into consideration that there are immense masses of people who live contrary to their dicta and still perform labor.

"Man has not the teeth of the carnivora; the length of his intestines is six times the length of his body; just as the ape, essentially fructivorous, has not a carnivorous structure. Moreover, a meat dietary is not as widespread as is supposed; it is rather the exception than the rule. Whereas the Englishman eats on the average 100 grams of meat per day, the Frenchman eats but 35 grams, and only the Frenchman of cities at that. If meat diet were much extended, the lack of meat would become an insurmountable obstacle. The number of domestic animals is diminishing, and if all those in existence today were slaughtered, it would furnish for each inhabitant of Europe 400 grams of meat for one year, and no more.

"All humanity may be divided into those who subsist on rice, on corn, on wheat, and on rye; the meat eaters representing a small minority."

If the opinion were correct that lack of meat as food is the cause of pellagra, then all humanity would be pellagrous, including the peasants of Sicily and Sardinia, who, for whole months, eat only lettuce and figs; and the Japanese, who eat almost nothing but rice, and rice contains even much less of hydrocarbons and albumenoids than does corn. It must not be concluded from this that these persons remain

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\*Revue scientifique, 1881.



Jacini, in his classic work on landed estates, says that in lower Lombardy, at the height of the summer, they give daily, to a domestic, 2 lbs. of corn; in winter 1 1-2 lbs., and in addition two to three measures of milk, two rice soups, and on Sunday sausages. The younger domestics have the same diet except the milk.

Calderini also says that out of the pellagrous sufferers visited by him, who took meat diet, 18 per cent. of the women, and 41 per cent. of the men ate meat on Sunday, 87 per cent. daily took milk, 17 per cent. took wine, and 33 per cent. wheat bread.

According to the facts noted in the report of Friuli, by the Engineer Camis: "In a population, which numbers 3 per cent. of pellagrins, each peasant consumes annually, besides 372 kilograms of corn, from ten to ninety kilograms of each of the following: beans, rice, potatoes, and other vegetables, pork and bacon, olive oil, fish, chickens and wine. They do not eat beef except on festal days, for a marriage or an illness, or when an animal of the herd dies."

In the province of Ferrara an adult hired peasant consumes on an average daily:

	Usually (eight months of the year.)	During severe labor (four months of the year.)
Polenta .....	1,000 grams...	160 grams.
Milk .....	Almost none...	Almost none.
Eggs .....	One-fifth .....	A half.
Onions .....	One .....	Two.
Wheat Bread.....	50 grams...	400 grams.
Macaroni.....	50 grams...	200 grams.
Meat (principally pork).....	10 grams...	60 grams.
Cheese .....	5 grams...	20 grams.
Beans .....	150 grams...	40 grams.
Fish .....	20 grams...	Almost none.

Apart from its readiness to undergo change, corn, from a physiological standpoint, is an excellent food. But experience has proven that even so good a food as corn cannot, without harm, be continued exclusively for a long time.

Agricultural experiments have shown, however, that animals fed on corn alone may fatten. For example, Guffart succeeded in fattening some hundreds of cattle on selected corn alone, although he found it much better to mix therewith forage or oat straw: 12 cows weighing 2,207 kilograms, attained, after being fed on corn alone for 156 days, 159 kilos per day, the weight of 2,951 kilograms. Eight cows, which in 453 days, had consumed 12,063 kilos of corn, along with 2,935 kilos of oat straw, increased from 3,549 kilos to 3,996.<sup>1</sup>

Dankoff has proven in his recent work that many ruminants perish if they are given the same food, as oats or turnips, for more than three months. That is due to the fact that the same food continued monotonously, surfeits and destroys the appetite; it is sufficient to change the diet and all danger is gone.<sup>2</sup>

Experience teaches us that the poorest laborer varies his diet on occasion of the smallest festival. One would therefore err if he pointed out as an etiological factor a diet insufficiently varied. It would be regrettable if the government, in fighting pellagra, should resort to the distribution of meat rather than establishing drying ovens and granaries for corn.

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<sup>1</sup>Manuel de la culture du maïs, 1879.

<sup>2</sup>Arch. Anatomie et Physiologie, 1881, p 433.

If it is claimed that corn does not contain enough of the essential nutritious substances, or, at least, that it contains them in smaller quantities than other cereals, an answer may be found in the following tables of Gühring, of Bell and of Koenig and Dietrich:

COMPARISON OF CEREALS BY GUHRING.

	Water.	Total dry substance.	Proteids.	Fats.	Extractive Substances (Non-Nitrogenous).	Potash and Soda.	Phosphoric Anhydride.	Cellulose.
Wheat flour . . . . .	13.6	86.4	12.0	1.1	72.3	0.173	0.249	0.5
Rice meal. . . . .	10.03	89.97	11.7	2.0	48.6	2.228	3.939	15.0
Corn meal. . . . .	10.0	80.0	15.2	3.8	70.5	0.220	0.306	....

[For comparison, the following table taken from Bell's analyses,<sup>1</sup> may be added:

CONSTITUENTS OF THE GRAINS OF THE COMMON CEREALS.

	Wheat (Winter Sown).	Barley.	Oats.	Maize.	Rye.	Rice.
*Starch . . . . .	63.71	63.51	49.78	64.66	61.87	77.66
Nitrogenous matter (i. e., albumen, cerealin, etc.) . . . . .	15.53	11.46	14.67	14.27	14.87	9.34
Cellulose . . . . .	3.03	7.28	13.53	1.86	3.23	Traces
Sugar (saccharine body allied to cane sugar) . . . . .	2.57	1.34	2.36	1.94	4.30	0.38
Fat . . . . .	1.48	1.03	5.14	3.58	1.43	0.19
Mineral matter . . . . .	1.60	2.32	2.66	1.35	1.85	0.28
Moisture . . . . .	12.08	13.06	11.86	12.34	12.45	12.15
Total . . . . .	100.00	100.00	100.00	100.00	100.00	100.00

\*The starch includes from 1 to 1.5 per cent. of dextrin, and together with cellulose and sugar, comprises the carbohydrates of the cereals.]

<sup>1</sup>Quoted from Kenwood—Public Health Laboratory work, London, 1908.

PERCENTAGE COMPARISON OF CEREALS ACCORDING TO  
KOENIG AND DIETRICH.

	Non-Nitrogenous Extractives.	Fatty Substances.	Protoids.
Rice .....	72.47	1.76	8.38
Corn .....	65.43	5.56	9.90
Rye .....	65.16	1.96	13.31
Wheat .....	68.85	1.55	12.66
Irish potatoes .....	21.	0.15	2.17

The opinion that corn is dangerous because difficult of digestion is without foundation. According to the above table of Koenig and Dietrich, and according to the demonstration of Uffelmann in his Hand-book on Hygiene, the nitrogenous substances contained in corn are very much more digestible than those of wheat bread, rye bread and Irish potatoes. It may be added that according to Letheby, the quantity of nitrogenous matter contained in oats, barley and rye has a value of 1.90 francs, while in wheat bread it has 2.21 francs, in rice 3.80 francs, in potatoes 2.77 francs, in milk 7.39 francs, in pork 8.87 francs, and in corn 1.08 francs.

PROPHYLAXIS.

From all the proofs given that feeding upon spoiled corn alone is the cause of pellagra, there would seem a very definite and certain means of prophylaxis.

To tell a peasant, as many do, that, if he wishes to protect himself against pellagra, he has only to have a good dietary, and then drink more wine, is correct; but this advice is useless, harmful and even cruel irony. When one treats pellagrins at home, it is

more difficult to nourish them with bread, meat and corn, than merely to give them counsel. They will continue to eat corn because they have no better, and cannot get any better; and the chances are that there is, in the corn they have, a variable but decided proportion of spoiled grain. If the unhappy peasants of Lombardy were able to have a better diet, they would have it without the advice of the physicians, says Lombroso, and they would not have pellagra. Good diet, however, will never eradicate pellagra. The first therapeutic effort in the treatment of pellagra ought, nevertheless, to aim at the suppression of the cause of the trouble, that is, the dietary of spoiled corn, a thing easy to secure in hospitals. Clinical experience and pathological anatomy demonstrate that pellagra does not come from lack of proteid in corn, but from the use of corn which has become spoiled. As we have already said, corn, in proportion to its price, yields a quantity of nitrogen larger than that of any other aliment with the exception of beans. [Pellagra is a morbid entity, entirely distinct from mere inanition.]

One should not, then, forbid corn to the peasant, but counsel him to harvest and preserve it in such a manner that it cannot spoil.

With regard to general prophylactic measures, various suggestions may be made. Ameliorate or change the various modes of corn culture according to the region; for example, the culture of *quarantina* may be suppressed where corn ripens badly or is harvested too soon and, therefore, does not

become thoroughly dried; the corn called "dwarf corn," or "chicken corn," which matures more readily, may be substituted for it. In sandy ground the cultivation of white corn, which does not grow well there, ought to be abandoned from economical motives as well as for hygienic reasons.

Intensive culture can be carried on only by means of irrigation, but then in certain districts watering costs from 25 to 50 francs per hectare.

If, according to experienced farmers, in the place of *quarantina*, potatoes were planted, there would be a more profitable crop. Irish potatoes yield 100 hectolitres per hectare; the *quarantina* only 36; then, the bad weather does not spoil the potato crop as it does that of corn; finally, if you reckon 500 francs for seed, and eliminate the fodder, the potatoes would still yield a greater profit by 100 francs.

Other writers recommend millet in the place of potatoes. It is very nourishing, but does not yield so well as potatoes and it exhausts the soil.

In regions where it rains regularly at the time of the harvest, there would be needed a place paved with good stones or with cement, with spacious room for storing the cereals after drying them in the sun. One could follow the example of the peasants of Mexico, where, after the harvest, they expose the grain to the sun during the day and put it under shelter again at sunset.

It would be worth while to set up co-operative machines for shelling, and in this way the corn of the small farmers would be as quickly shelled as that of the large proprietors, without being more

exposed to inclement weather. This would mean economy in wages. On the small farms it would be sufficient to have movable frames for exposing the ears of corn to the sun, as is done in the Tyrol, Tuscany and Liguria.

The system of preservation ought to be completely changed. In most of the great public or private granaries of upper Italy, they should make general use of the means which, in the approval of all Europe, preserves the corn from dampness, fermentation, mice and worms, and which considerably diminishes the losses during preservation.

To the apparatus of Devaux is due the freedom from pellagra enjoyed by the Irish, who, in later years have to some extent substituted the use of corn for potatoes in their dietary. This apparatus consists of a series of light iron frames or boxes, 15 meters high and 1.67 meters wide, each perforated by small holes like a skimmer, and the whole traversed from below upward by a tube or cylinder likewise perforated. The grain, through which the air must pass, is never placed in layers deeper than 65 to 70 centimeters, so that the air may easily percolate. The air is heated and pumped through the apparatus by means of steam. While with ordinary methods of preservation there is expended from 1.50 even to 3 francs per hectoliter without obviating a loss of 8 per cent. to 16 per cent. through spoiling of the grain, or through the evaporation which follows heating, yet with this apparatus preservation costs only 7 or 8 centimes per hectoliter, and there is no greater loss in the weight and value of the grain.

The Pavy granary renews the air, dries and cleans the corn at a cost of 1.50 francs per hectoliter. For large landed estates the granary ventilator of Valery is suitable.

Similar apparatus ought to be installed on board those ships which transport cereals, and on which corn is piled up unprotected and exposed to rain. A great increase of pellagra in Italy, in 1853, was due to corn imported from Odessa, which was exposed to continuous rains during transportation.

In regions with a dry soil the corn containing less than 16 per cent. of water can be preserved in tight receivers communicating with the air (silos of Romagna). The millers and bakers could use very simple arrangements like the screens used in Mexico.

New industrial applications for the use of corn other than its use for human food should be encouraged. For example, the manufacturing of spirits or alcohol, and above all, the feeding of stock.

Premiums ought to be accorded to inventions which improve the baking of corn bread and its preservation in the ordinary bakeries.

Laws ought to forbid the grinding and selling of mouldy corn. Oversight ought to be organized in the country at the time of harvest, and in the cities over the great warehouses at the time of summer heat. Severe fines ought to be prescribed against the proprietors who oblige their laborers and small farmers to eat spoiled corn. These prohibitions were already in force in Venetia as early as 1776 (See Appendix III), and are still so in Austria. But



in consequence of acquittals, a fine for selling spoiled food does not attain its end, and indifferent public opinion neutralizes the good effect of the laws.

There should be established cheap coöperative bakeries among the peasants whereby they may protect themselves from dishonest bakers and millers. But perhaps a better method might be the adoption of some new process of preparing and cooking corn similar, for example, to that used in Mexico (*tortilla*) and in other countries.

Treatment should be begun early in all cases, and as soon as the first gastric and nervous symptoms develop, the patients, if adults, should be given arsenous acid, and, if children, sodium chloride. In early cases symptoms yield readily to treatment and cures become difficult when the case is neglected for too long a time. Would it not be in the economic interests of the commune to aid in establishing such things as small provisional hospitals for early treatment of these cases, and the consequent prevention of hereditary diffusion of the disease? These individuals, in this case, with the expenditure of a few lire, or even at times a few centesimi, might be saved to discharge their duty to society instead of perhaps remaining helpless burdens which may ultimately cost the commune hundreds of lire? It is worthy of note also that the Austrian government has adopted measures of this kind to aid pellagrins in their own homes.

In some conditions, as after severe inundations, for example, when the inhabitants might be forced to live on spoiled corn, nothing would remain but to

counsel depopulation of the region by means of emigration, if necessary, to other more favored places, even to America.

The sons of pellagrous parents might be sent into the army or advised to emigrate to other countries which are free from pellagra.

Finally information with regard to prophylaxis and treatment should be disseminated among the agricultural classes. Much can be done in this manner. (See Appendix IV.)

Roussel, in his work, formally accepted spoiled corn as the cause of pellagra, and was the first to spread in France the ideas of Balardini. Later a physician of the department of the Hautes Pyrénées, Costallat (1857), became the ardent and convinced defender of the "verderamist doctrine." "Pellagra is a slow poisoning by *verderame* or *verdet*," said he in reporting the presence of the parasite on the corn in the markets of Bagnères-de-Bigorre.

These demonstrations and the different campaigns, which popularized them, have succeeded in France. The experimental demonstrations have been repeated by Balardini, Ellia and others, either with the grain of spoiled corn or with polenta made from such grain; young chickens fed on it refuse to eat, lose weight, become droopy, tremulous, and very thirsty; at the end of twenty-eight days they are in the last stage of exhaustion and moribund. In Ellia's experimental chickens the feathers, moreover, became roughened and the skin became the site of a furfuraceous desquamation.

Lussana and Frua injected into the veins of dogs and of birds, the powder of corn, affected by *verderame*, mixed with water; at one time the aqueous extract of this substance; at another, finally, the very fine powder of *verderame* itself. Most of the subsequent symptoms observed, such as dyspepsia, coagulation of the blood, pulmonary ecchymoses, vomiting, congestion of the liver, and intestinal inflammation could be attributed to the severity of the experiments, but not so, the apathy, clonic convulsions and paralysis, more or less complete, especially of the hind legs, which are observed in the dogs that, for a time, survive the initial intravenous injections. These phenomena show characteristics too marked to be misinterpreted.

Leplat, Jaillard and Lombroso have shown that the injection of *Penicillium glaucum* is harmless, provided the injection is so managed as not to produce capillary embolism.

Since then, Grawitz has claimed success in the production of infectious properties in *Penicillium glaucum* and in *Aspergillus glaucus* by appropriate cultural methods. Graffky and, later, Schultz, in the laboratory of R. Koch, convinced themselves that the foregoing investigator had been deceived. *Aspergillus fumigatus*, *A. Flavescens* and *A. Niger* are dangerous moulds, but they concern only pulmonary mycosis, and not general infections. There is also recognized a toxic *Mucor stolonifer* or *Rhizopus nigricans*, which forms the black mould of wheat bread. This, also, it would seem, is not to be incriminated.

Tizzoni, Panichi and Fasoli have isolated and cultivated a specific micro-organism common to typhoid pellagra, to pellagrous insanity and to ordinary chronic pellagra, in different and remote localities. They found it in all the principal viscera and in the central nervous system; they cultivated it and injected it into animals, obtaining morbid experimental symptoms analogous to those of severe pellagra and also nervous and typhoidal symptoms. The meninges, the cerebro-spinal fluid and the blood in severe cases of pellagra have been subjected to culture with success by these authors, who describe a specific diplococcus found in the viscera, especially the intestines, which enters the circulation and through its toxins later involves the nervous system.

[Tizzoni's work has already been discussed in the chapter on etiology, *q. v.*]

The researches of Lombroso opened a phase entirely new in the struggle against pellagra, from the all important standpoint of the etiology of this scourge. As has been said, the discoveries made by Lombroso advance along the same lines as the very interesting observations of A. Gautier, Selmi (of Bologna), Brouardel and Boutmy, relative to the formation and the properties of cadaveric alkaloids—the ptomaines. The question here seems to concern alkaloidal bodies, which, if not ptomaines, are, at least, closely allied to them.

[The nature and origin of these toxins is naturally of paramount importance to the Zeist idea.]

Selmi has formally applied to spoiled corn the procedure used in the investigation of the ptomaines. It is a great honor to Lombroso to have taken up and sustained, by experiment, the pregnant idea of his illustrious compatriot, Balardini, which others blushed to hear called "the Italian doctrine."\* The assent of Husemann and Cortez, and of Félix (of Bucharest) and of the authorities assembled at Genoa in 1880, Manassei, Schilling, de Pietra-Santa and others, have in large measure compensated the Professor of Turin for the rather hasty judgment, in 1875, of the Commission of Lombardy Institute.

Besides corn, other cereals, such as wheat, rye, oats and millet, denounced by Faye, are susceptible of being invaded by fungi before or after the harvest, as Bouchut has remarked. From such cereals intestinal disturbances may arise which are more or less pellagroid in their nature. If corn, which is an exotic plant of comparatively recent introduction into Europe, and which has not yet acquired the power of adapting itself to environment as has wheat, is to be grown in various localities, and remain free from deleterious change, then it will be necessary to find upon our continent conditions of soil and climate which approach that of its native land. Unless this is done the grain will never arrive at perfect maturity, or only arrive at it in a state of uncertain vigor, not actually diseased, perhaps, but easily subject to general or specific morbid influences. It seems, indeed, that everywhere, Mexico included, the grain of corn has a delicate germ,

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\*Scientific Congress of Paris, 1867.

badly protected by its envelop, incessantly menaced by dangers and atmospheric influences. Even in Central America there is need of having it properly stored, and still it is not eaten until it has been carefully prepared.

It is probable that it was the object of especial care at the time of its transplantation to Europe as a rare and valued plant, but since then the farmers have strangely relaxed and corn is cultivated on all sorts of soil. No attention is paid to the better varieties most apt properly to mature, but concern is given only to those which give the greatest yield; and advantage is taken of the rapid growth of some varieties to sow them even when summer is closing, as if corn were not a plant of warm countries.

The principal varieties of corn cultivated in Italy are:

- (a) Summer Corn (*zea mays vulgaris aestiva*);
- (b) Autumn Corn (*z. m. autumnalis*);
- (c) Quarantina Corn (*z. m. praecoë*); (40-day corn);
- (d) Beak Corn (*z. m. rostrata*);
- (e) Cinquantina (*z. m. sub-praecoë*); (50-day corn);
- (f) Dwarf Corn (*z. m. minima*);
- (g) White Autumn Corn (*z. m. autumnalis leucosperma*);
- (h) Red Corn (*z. m. rubra*).

White corn succeeds in clayey soil, but only the yellow variety can be cultivated in sandy soils.

One of the great advantages of corn for rural populations is the fact that certain varieties can

be sown as an after crop in a field which has already yielded, in the same year, a harvest of rye or legumes; but in this case it cannot be planted until the end of June or July. It is necessary, however, that it mature early enough to be harvested before the bad weather. If it is not cut by the middle of September, there is great risk of its being stored damp. The grain of the variety called *sessanta*, or "60-day corn," which requires two months for maturing, cannot be harvested before the end of September, and is almost always stored unripe and permeated by dampness. Furthermore, after cutting, it does not dry readily upon the ground, because the days are short and rainy. The conditions are particularly bad when the peasants, induced by the large yield, have sown in the mountainous regions either this variety, or even the *cinquantina* (50-day corn.) The varieties *zea mays aestiva*, and *z. m. autumnalis*, which require four to five months for maturing, frequently produce crops which have been soaked by the rains while ripening in the field. These are, however, the preferred kinds, in Umbria, for human food, the early varieties being cut green for forage.

The poor system of crop rotation, followed in upper Italy, has been censured (Roussel, Lombroso), probably with reason; because corn, like every other vegetable growth, loses in quality if it is planted on the same ground several times at short intervals. The summer and autumn corn occupies the land nearly all the season.

The unripe and damp grain could, with a little effort, be improved and preserved, if it were placed in thin piles in dry granaries, and well aired. This was formerly done when the cultivation of corn was important; but today too much is harvested to give the crop the necessary care; it is piled up and becomes heated. White corn, very much cultivated in Moldavia and Wallachia (Roumania) is particularly subject to alteration.

In Italy there is used not only home-raised corn, but imported as well. There are merchants in Umbria who sell great quantities of corn brought in from Albania, and also from the Danube provinces. and Venetia. Some is landed at Ancona, which comes from the orient in coasting vessels, especially from Albania and also from the Danube provinces. Though it is damaged and several years old, trade, nevertheless, keeps it going, and it is here that the millers come to the aid of the merchants by mixing bad meal with good. Lombroso, by concealing his identity as expert and philanthropist, easily found dozens of samples of rotten corn in the stores of the merchants of all the regions of Italy. These grain dealers know how to disguise the defects of their wares.

Thus spoiled corn is common in Italy. But who eats it, and especially who eats it almost exclusively? Not the farmers in easy circumstances; these eat other cereals with the corn, and, furthermore, the corn is of good quality; the macaroni of which they make soup is made largely of wheat flour. They introduce into their diet rice, potatoes, cheese, oil,



fat, sometimes meat, or fish when they dwell near a lake or the sea. Many drink wine. It has been remarked that the cantons, where formerly wine abounded, have become pellagrous since the *oidium* has restricted vine-growing.

Those who eat scarcely anything but corn, receiving it in a spoiled condition during most of the year, are the poor laborers of the fields, whose existence is at the mercy of the landed proprietor or of the large farmer (*affittatore*) employing them. In Italy the landed estates are rarely divided, the land belongs to great lords, who usually live in the cities, as in England and in Ireland. The land owner rents out large tracts to a middle man, who, in turn, sublets portions to families of laborers (*coloni*). Each family pays him regularly in kind, in proportion to the amount of land they have in charge; he employs them, furthermore, at various kinds of work at poor wages. This is the system called *affittanza*, the most widely spread in upper Italy, and which is oftenest met with in the cantons afflicted with pellagra. It is through this system, says Senator Jacini, that one realizes the strange association of enormous production with the poverty of the producing class. Except in especially favorable seasons, when the renter has paid his land rent, selling his rye and wheat to pay such rent or to meet divers expenses of the family, there remains to him only corn enough to last till the next harvest. This makes living very hard, as may readily be understood. Often, towards the end of winter, the renter having no corn whatever left, must borrow from the

farmer, who gives him the poorest quality, and for this he must return sound grain after the next harvest. The system of *mezzadria*, or farming on shares, is but little better than the preceding. The proprietor himself divides his land into small portions; the share farmer, who takes one of them, owns at least the cattle and farming implements; he is something more than the slave of the *affittatore*. Nevertheless, many of the *mezzadri* are pellagrous; they scarcely use more than 1,000 to 1,800 grams of corn per day in the form of hard, badly cooked cakes, with various legumes. As for the simple farm hands, it is common for corn to be their only daily food, and what spoils in the master's cribs falls to their lot. But it is necessary to live! These wretched people know in advance what awaits them: *O, mangiare questa minestra! O, saltare questa finestra! Cioè andarsene via.* [O! to eat this soup! O! to jump out of this window! Either is suicidal!]

A man named Giardini, according to Lombroso, brought dying to the hospital, stammered out: "My trouble is rotten polenta!" When cured, he stated that he and a dozen hands on the Bisone farm, had been fed for six months on corn beaten down in the fields by hail; and as the cattle would not eat it, men were compelled to do so.

It is in this way that upon the most fertile land of the world, the plains of Lombardy and the valley of the Po, an entire class of the people is forced to live on produce fit only for the refuse heap.

Many peasants mix spoiled with good corn, thinking they will be safe because of the good therein. Some eat who do not wish to confess it, fearing to be

accused of carelessness in gathering the harvest, or of having stolen it from the stalks of the master before it ripened (Lombroso).

When the corn has become toxic, Lombroso says, neither parching nor the action of alcohol nor superficial boiling succeeds in freeing it from its injurious properties. To do this would require boiling at 120 degrees C. with quick lime, then drying in an oven, a fact which explains why polenta and corn cakes made of spoiled grain remain injurious.

These two preparations, polenta and cakes, are, by far, the commonest forms in which corn is eaten. Although corn bread (yellow bread, *pane giallo*), has in it almost always a little rye meal, about one-tenth, it is not easily digested on account of its compactness, and so all writers condemn it even more than polenta or corn meal gruel. Corn enters into the *minestra* (which is a soup) either in the form of meal or in the form of macaroni (*pasta*).

Formerly in the departments of southwestern France, the field hands ate a greater variety of corn products, alone or mixed with other things, than they do today. The regular preparations were: the *méture*, *mesture* or *mesturet*, made in Béarn with corn meal and water, mixed to a dough, and baked in an earthen pan in the oven; the *cruchade* of the Landes, more often made of millet meal prepared as the preceding, but baked in a plate, which renders the cake thinner, better baked and more easy to digest; the *miques* or *micoles*, balls of corn meal dough, to be added to pork soup; the *broye* (in

Béarn), *touradiso* (in Bigorre) or corn dough; the *hariat*, corn dough for soup made with cabbage and grease ( Lourdes); the *miliasse* and the *tougnos* (Lauraguais), thin corn cakes, with salt and sometimes with honey.

At the time of the journey of Roussel and the researches of Costallat, aggravating agricultural blunders were seen in the French provinces of the southwest, as in upper Italy; the crop rotation which every two years permits the replanting of corn upon the same field; the cultivation of white corn, and of slow growing varieties; the same relations between the proprietors and laborers, the share system of farming and the *estivandiers* (boss-hands); the most numerous class compelled to eat the cheapest food, and, consequently, of the worst quality. Indeed, the peasants ate corn so much that they had to bring in additional supplies of it from Armagnac; and this corn proved to be so much damaged that only the very poor ate it, while people in easy circumstances fed it to animals (Roussilhe). In the Landes, particularly, they usually cultivated the variety which is planted in June or July in fields which have earlier in the season already yielded a crop of rye.

The *mamaliga*, which the Wallachian peasants regularly eat, is a corn gruel like polenta (Schreiber). The Roumanians also harvest their corn before maturity and pile it in silos where it easily ferments.

Experience shows that the people who eat corn perfectly matured, well preserved and protected

from dampness, do so with impunity. It is, therefore, necessary to recommend the varieties which rapidly mature, especially *quarantina* corn. Directions should be given for early sowing, and not after the previous harvest of some other crop. Advice should also be given with regard to diversity in crop rotation so as not to permit the planting of corn on the same land without an interval of three or four years. The topping of the ear to hasten maturation complicates the work and probably would be neglected or be impossible in cultivation on a large scale. Corn harvested before the rainy season ought to be dried in the field or the ears hung up with open shuck in a high granary, dry and airy, as is done in Franche-Comté and in Burgundy. The grain ought not to be left in large, but in small piles.

In Bresse, in Franche-Comté, and in Burgundy, says Perrusset, of Macon, after having gathered the ears the shuck is drawn back and two piles are made. The ears intended for meal, which is to be made into cakes, are exposed to the air, suspended by the shuck which is left on the stem, under the shade of the farm buildings or in the interior of the apartments. When the corn is thus well dried, it is shelled for grinding. The corn intended for *gaurdes*, red gruel and polenta, is subjected to a kind of drying process. Then there is also corn called *fournayé* (dried in the oven), to use the expression of the country, and it is made into meal. Meal of corn thus dried has a very agreeable odor. It is especially in this form that corn is used for food in the previously mentioned countries (Roussel).

Thus it is before the formation of verdet that corn should be dried and heated naturally or artificially. When the moulds are developed, it is too late, since the poison, which is now no longer a fungus, resists the boiling temperature. This would indeed kill the fungi, and, perhaps, their spores; but it does not destroy the properties of the alkaloidal bodies, once they are formed. The distinction is important and it is a precious gleam of light which we owe to Lombroso.

In southern America, as in Mexico, according to Parmentier, care is taken to sun the newly gathered ears and put them under cover for the night, and never to put them in piles. When they are ready for shelling this operation is carried out and the grain dried again in the sun. Corn meal does not demand less care, being even more easily affected than the grain.

Within the limits of the possible, it is necessary to abandon by degrees the practice of using corn meal in the form of bread, cakes, *cruchade*; even when mixed with rye it is only with difficulty that a trustworthy product is obtained in these forms. The peasants, unskillful or negligent as they are, obtain from it only a food, which is hard, glutinous, indigestible, and difficult of preservation. The Mexicans avoid eating corn in this state; it is almost always gruel (*atole*) that they make. It is true that they have a cake called *tortilla*, which plays a large part in their daily diet; but this is prepared in a manner which deserves to be noted. They commence by adding to water in a vessel sufficient slaked lime

to make a thick gruel, then corn in full grain is boiled in this for eighteen hours. At the end of this time the corn is taken out, washed carefully in clean water, and afterwards crushed by kneading to make a dough which is then formed into cakes. These are baked on a hot iron griddle and turned often during the baking. Enough gas is formed in the center of the dough to cause it to swell and make the bread light.

There is evidently a great moral awakening to be wrought among the populations of southeastern Europe by general education and instruction in dietetics. The prophylactic measures advised for all these provinces, by the Commission of Inquiry of 1879, is: "Amelioration of the condition of the peasants, the introduction of meat and wine in their dietary." The advice is good, but how shall we put it into practice in the present state of land ownership in these districts, and under the existing agricultural, economic system which the victims thereof are unable to reform? The intervention of the state with protective measures, by the organization of sanitary surveillance, would perhaps be proper. On this delicate ground the question of hygiene joins hands with the sociological question. Everywhere there should be supervision of the trade in food stuffs and the sale of spoiled corn ought to be prohibited. Wherever the monotony of living on corn alone is broken by the use of some other food, which counter-balances its effects, pellagra has diminished or disappeared.

Meat, milk, wine, fish, cheese and even potatoes and legumes, these have proven to be potent for prophylaxis always when the peasant has been able to substitute them more or less completely for corn in his daily diet. The importance of favoring variety in the cultivation of crops, and of using some economical inducement to this end would then seem to be indicated. On the other hand we possess henceforth in Europe the means of equalizing our lack of meat by purchasing, cheaply and in a good state of preservation, the surplus of the New World and of Australia.

In France where the division of the landed estates permits the peasant to acquire individual ownership, pellagra has disappeared, for example, from the Landes. How did this happen? They made of a marshy waste a rich and fertile country by the exploitation of the seacoast pines, and by the cultivation of the better cereals, even of the vine, all accomplished by the marvelous works of drainage, which are the glory of the government of that region. Fever rapidly disappeared, and this is always a blessing and is moreover an indirect guarantee against pellagra. Corn is still cultivated, and is even still eaten; but it is, in part, given to the stock; and, if it is used for human food, there is added wheat or other cereals, legumes, and also meat and wine. The peasant of Landes now eats meat several times a week, and drinks wine, if not of the first quality, at least an alcoholic drink made with malt, raisins and corn sugar. A good part of the corn is transformed into sugar in several factories. Today the Landes



has railroads, which guarantee the transportation and exchange of food stuffs of all sorts. Intelligence, the will of individuals, the aid of the local government, such are, if not the entire prophylaxis against pellagra, at least the instruments of this great work. "With a little good will on the part of the landed proprietors," says Senator Mantegazza, "and also of the better class of peasants, it would be possible in a half century to abolish pellagra." "Pellagra ought to disappear and this new disease enter into the category of extinct maladies" (J. Arnould).

### ROUSSEL AND LOMBROSO.

In 1907, a monument to Théophile Roussel was unveiled in the Avenue de l' Observatoire, and eloquent orators delivered addresses.

The career of Roussel, the statesman, was recalled, also that of the philanthropist, for to him are due the laws of the 4th of February, 1873, against drunkenness; those of the 23d of December, 1874, for the protection of children and the law in regard to delinquent children. He exercised much influence over the passage of the law of 1893, upon free medical aid, as also upon the reports of the senate relative to reforming the law of 1838.

But one fact which nobody recalled—his first feat of arms on a field of public charity and hygiene—was his battle against pellagra. At that date, in 1845, it was a living question in France; today not only the disease, but almost the very name of it, has been forgotten, since, thanks to him, its ravages have practically ceased.

Roussel recognized that pellagra is "a chronic intoxication, characterized, essentially, by a scaly erythema limited to those parts most exposed to the action of the heat and light, a chronic disturbance of the digestive tract, of which the most usual index is an obstinate diarrhea, and finally by a lesion, more or less severe, of the nervous system, terminating sometimes in mental alienation and paralysis."

Roussel contributed his part in showing that the cause of this intoxication lies in a food poison contained in spoiled corn, and that it affects those people who use such products for their food.

In Europe corn is a relatively recent addition to the human dietary, having been imported there about 1700 [?]. Pellagra made its appearance soon afterwards, and wherever the cultivation of corn as a cereal has extended, pellagra has followed in its wake; and has in turn disappeared coincidentally with the abandonment of corn as human food, or with the institution of the necessary precautions against moisture and decomposition of the grain, of the meal or of their cooked products.

At the time when Roussel commenced to sound the cry of alarm in France, pellagra in Italy had been the subject of special studies by Strambio and by the coterie of Italian clinicians who followed him. It is known that polenta, made from corn meal, is still the principal food in certain parts of Italy and Spain; and various national dishes are prepared from corn. Accordingly, pellagra makes fearful ravages in these countries. Two per cent. of the population of certain agricultural districts of Spain

are said to be affected, and in Italy there are still (1908) nearly 80,000 pellagrins notwithstanding the crusade which Lombroso, following the example of Roussel in France, has led against it.

At last there has sprung from these efforts special legislation, which regulates the hygienic condition of the granaries and corn transports, the supervision of the special markets, the control of foodstuffs of this kind, and seeks the suppression of fraudulent methods. But numerous congresses and a unity of effort on the part of experts and public officials has been necessary to repress this evil.

In France, the Academy of Medicine, stimulated by the first work of Roussel, supported his demand for a commission to study the matter in Spain and in Italy. From this resulted a series of debates and finally investigations in the district of Landes, the people of which at that time were suffering from pellagra. To these circumstances we owe the important studies of Roussel on this disease.

At his visit, in 1844, to the afflicted districts mentioned in the report of Léon Marchand, he found conditions somewhat improved, and the disease appeared to him to be less serious than had been reported. In a general way the disease seemed to show some connection with deplorably inferior food, and, more especially, with the use of corn which had been harvested under conditions favorable to moulding.

In Landes, Roussel obtained useful information from physicians in active practice, whose names should not be forgotten: such are Dejean, Courbin,

Gazaillan, the two Bergerons, Lemaire (of Mimizan), Gazaban (of Aurice), Lestelle (of Cauna), Comin (of Sos), Dabos and de Calvière (of Gabaret). It was at Mimizan that Roussel first heard popular names of pellagra, some of which have been the occasion of much dispute; for example, Mal d'Arrousé, de Saint-Amans, de Bascons, de Sainte-Rose. The last two are taken from certain places of pilgrimage commonly visited by the sick; the name mal de Saint-Amans is only a corruption of Saintes-Mains, the anointed hands of a certain colossal crucifix, from which the pilgrims took salve wherewith to rub themselves.

However, in 1847, pellagra was reported by the doctors Roussilhe (of Castelnaudary), and Calès (of Villefranche) in a second locality in France, not far from the first, in the country districts of Lauragais. Roussel used the occasion of his journey to verify the facts. Here, without possible error, was pellagra again, and, to all appearance, pellagra from the poisons of corn. Finally, the departments of Hautes and Basses Pyrénées were reported as a third disease center; and as Dr. Dozons, of this region, had, in 1845, protested against the conclusion of Roussel, reached on the very ground where corn is cultivated, the learned pellagrologist made a visit to his critic in the Pyrenees. It was seen, without difficulty, that the quarrymen of Lourdes, who use a great deal of corn, but of very good quality, were not suffering from pellagra, but certain peasants of the neighborhood were victims of it. On the other hand, the disease appeared at Cauterets, in the Can-

tons of Nay, of Claraq and of Arudy, and extended even into the Canton of Pau (Gros, Pomès, Suberbielle, Fourcade, Darthez, Gazaban, Juppé, Pétrique, Talamon), always in connection with an extensive use of corn, and by reason of the poverty of the inhabitants, most often corn of the worst quality.

Later (1855-1857), in this same region at the foot of the Pyrenees, Costallat (of Bagnères), together with Verdoux (of Labassère), Duplin (of Laborde), Pédebidou, Lacoste (of Ibos), confirmed the diagnosis of pellagra, and showed, by exact facts, its connection with the eating of spoiled corn. The work of Costallat was the occasion of a report by Duplais (1858) to the council of hygiene of the Hautes-Pyrénées. The disease, regarded therefore as an obscure malady, known only to transalpine travelers, was all at once proclaimed as widely spread in France. Up to then the people did not know how to recognize it, or, perhaps, it was hidden under false diagnoses. But the time had come when, despite the lack of any real scientific knowledge of the matter, the disease was found everywhere, just as now is found widely prevalent the typhoid fever of Louis, the endocarditis of Bouilland, the disease of Bright, the paralysis of Duchenne, etc. Landouzy, director and professor of the clinical school of Rheims, found cases of it, especially in the poor houses, a prey to vice and uncleanness, and to physical and moral miseries. The eminent director of the clinic himself described the special symptoms of the different types and showed to his students not only pellagra without direct connection with corn

(hereditary pellagra), but pellagra without poverty, pellagra without nervous troubles, typhoid pellagra, etc. (Roussel). Under the influence of the same movement, Ch. Bouchard also discovered pellagra in the Hôtel Dieu of Lyons, and in the infirmary of the poorhouse of Rhône. Harmon, a pupil of Landouzy, brought to the attention of the faculty of Paris nine cases in sustaining his thesis (1861). Bourgade (Clermont-Ferrand) published two cases. The physicians of Paris, themselves, found some cases of "sporadic pellagra."

The Academy of Sciences, in 1865, crowned that work of Théophile Roussel, from which a large part of this chapter is taken. Landouzy and Bouchard have also studied the complex symptoms of this poisoning, more and more difficult to find in France, now that the cry of alarm sounded by Roussel in the middle of the nineteenth century has borne its fruits, and the use of the corn as human food has been largely abandoned in France.

The author found in Egypt a situation as lamentable as that among the agricultural populations of Italy, and of southwest France at the commencement of the nineteenth century. Roumania and southeastern Europe are still poisoned in this way, and will be for a long time. The recent uprising of the Roumanian peasants is directly associated with their wretchedness in which pellagrous poisoning plays no small part.

Régis, at Bordeaux, and Mairat at Montpellier, have recently (1908) made an investigation which concludes the series of studies on pellagra in France,

for it shows that pellagra has lived its day, and that there remains only the vestiges of hereditary taint manifested by mental troubles, erythemas, etc., occurring in a generation who have never eaten corn, but whose parents were poisoned by it.

The asylums of Auch, of Montpellier and of Pau contain still some survivors of the terrible pellagrous insanity, which Roussel has, so to speak, dried up at its sources, by announcing its cause; and, with the assistance of the medical corps of these regions, by influencing the people to give up this food product. The industrial improvement among the people has completed the work of liberating France from the use of a cereal now abandoned to animals. Let us hope that the vine growers' crisis and its miseries will not replunge the south of France into these distresses.

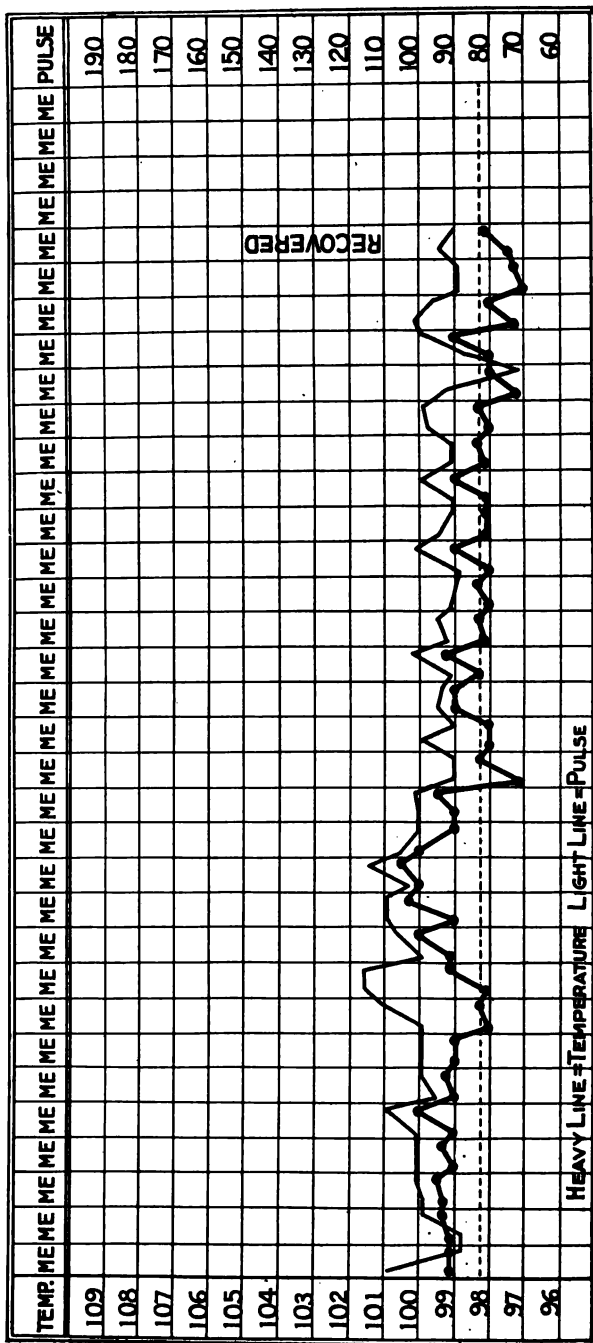
The writer believes that it is not without interest that he has recalled this page in the life history of a good man, who has, among other merits, the glory of having so completely delivered his country from this scourge that even before his death the people had almost lost the memory of it.

Less happy than France, in this respect, Italy still suffers from the terrible scourge of pellagra, though having blazed out the way leading to an unwearied scientific crusade. At the head of the present movement we must recognize Professor Cesare Lombroso, from whom we have borrowed the essential points for the writing of this book, which is but a feeble reflection of the enormous labor of a long life. For Lombroso consecrated a large part of his life to the fight against this cause of degenera-

tion so prevalent in his beautiful native country. More tried than France by international disturbances of war, followed by internal crises, Italy, in the course of the miseries of the century, has especially suffered from pellagrous poisoning. Like all the social poisons, this has been a disease of poverty closely dovetailed with the social evils from which she is freeing herself by degrees. As did Roussel for France, so in Italy, Lombroso has shown how to direct successfully the work of social redemption. If it is less complete, it is because the disease was deeper seated than with us; and if France was the first to free herself, this was due to the cry of alarm in Italy, whose echo Roussel caught and resounded in his own country. To Italy and her scientific leaders public acknowledgment is due. To Lombroso, particularly, the illustrious philanthropist and master, who has kindly permitted me to epitomize his great work, the writer owes this acknowledgment.

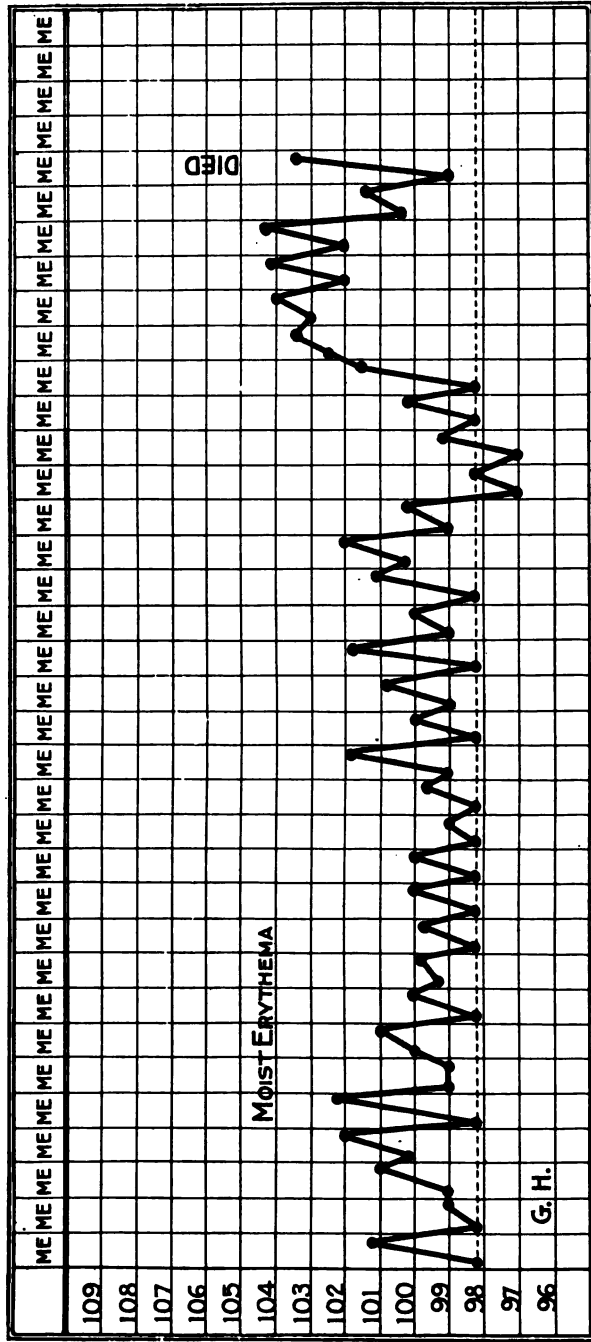






**Chart I.** South Carolina Case. Rather severe. Common temperature curve. Courtesy Dr. J. J. Watson.





**Chart II.**      **South Carolina Case.**      **"Wet" dermatitis.**      **Variable temperature.**      **Development of cachexia.**      **Death from exhaustion.**



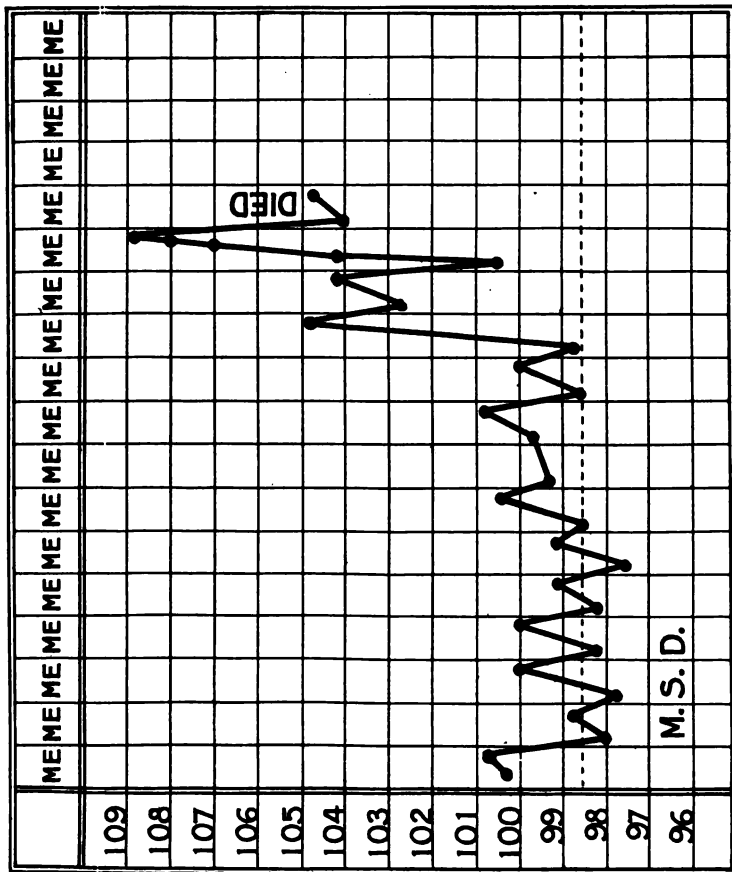


Chart III.  
South Carolina Case. Three years' duration. Terminal acute delirium with hyperpyrexia.  
Death. Courtesy of Dr. J. J. Watson.









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## APPENDIX I

### ITALIAN LAW OF JULY 21, 1902, FOR THE PREVENTION AND CURE OF PELLAGRA.\*

ARTICLE 1. All persons are forbidden to sell, to keep for sale or to distribute in any form or to any one:

(a) Indian corn that is immature, not well dessicated, mouldy or spoiled in any other way, whether in the form of grain or of meal.

(b) All products obtained from such meal and those which, although prepared with normal and sound meal, become subsequently mouldy or otherwise spoiled.

ART. 2. All persons are forbidden to introduce into the kingdom for use as food, corn or the products of corn that are spoiled or imperfect, even if the damage has occurred during transportation or in the warehouses.

ART. 3. The circulation in the kingdom, or the grinding and utilization of spoiled or imperfect Indian corn and its products for other uses than human food are subject to the authorization of the prefect, or of the local authorities, under conditions fixed by special regulations. The lack of such authorization will lead to the immediate confiscation of the goods, in addition to the penalties established by law.

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\*Appendices I and II are from an unpublished report to the Department of State on "Pellagra in Italy," by Vice Consul W. Bayard Cutting, Jr., from Milan, November 2, 1908.

ART. 4. Offences against the three foregoing articles must be reported to the judicial authorities by the officers and agents of the police and shall be punished by a fine of not less than L.51 and not more than L.2,000.

The sanitary officer of the commune, as well as the mayor and the provincial doctor, shall report directly to the judicial authorities, offences against the present law and the corresponding regulations.

ART. 5. The proceeds of the fines shall go to the benefit of local institutions for the prevention and cure of pellagra.

ART. 6. The sanitary officers and inspectors shall have the right to visit the warehouses of dealers in grain and flour and the workshops of millers, bakers and pastrycooks, in order to ensure the observation of the present law.

ART. 7. Every case of pellagra, even incipient, must be reported in the manner directed by articles 45 and 47 of the law of public health of December 22, 1888, No. 5849.

ART. 8. The communes where endemic pellagra has been certified shall be subjected to the special rules of article 9 ff. of this law.

The declaration of the application of these articles is to be made by decree of the prefect, under the advice of the provincial council of health. The decree goes into effect on the day of notification to the mayor, who is obliged to publish it on the self-same day.

ART. 9. In the communes declared affected by pellagra, the dessication, the preservation and the

consumption for food of Indian corn and its products shall be subject to the inspection and direction of the government and local authorities. The provisional laws for the immediate execution of this and the following articles and the special regulations for enforcing them in a permanent manner shall be approved by the joint provincial administration, after hearing the provincial board of health and also the agrarian committees and other agricultural institutions legally existent in the province.

ART. 10. In those communes that are declared to be infected with pellagra the prefect, after taking the advice of the provincial council of health and, where one exists, the provincial pellagrological commission, may order the construction or acquisition of one or more dessicating machines for Indian corn, of capacity corresponding to the local needs. Their use is to be regulated by the rules prescribed by the regulations for the execution of this law. The prefect may likewise direct the commune to appoint a place where corn, being the private property of inhabitants not possessed of healthy store places, may be kept for them under hygienic conditions, in quantities adequate to the family needs for private consumption.

ART. 11. The communal council shall make and keep a list of poor "*pellagrosi*" whose families cannot afford to supply them with a curative diet.

The provision of curative food for the poor who are suffering from pellagra is obligatory.

ART. 12. The indigent sick, for whom the insufficiency or inefficiency of curative diet has been ascer-

tained must be taken to institutions, hospitals or other suitable places.

ART. 13. The expenses accruing from articles 10, 11 and 12 are to be defrayed by:

- (a) Private beneficence.
- (b) The help of public institutions.
- (c) The proceeds of fines (See Art. 5).
- (d) The aid of the commune and the province, in the proportion of one-half from each.
- (e) State subsidies.

The assistance obtained under (a) and (b) shall go to diminish the consumer's share of the expense.

ART. 14. In order to assist the local authorities in the application of the present law, provincial and local committees or "Pellagra" commissions may be constituted in the manner decided by the special regulations. To them may be delegated special work for the prevention and cure of pellagra, as well as for the introduction of better agricultural methods.

ART. 15. In the case of refusal or hesitation on the part of any commune in the fulfillment of the obligations imposed by the present law, the prefect shall act with the power delegated to him by the provincial and communal law, with the aid, whenever needful, of the united provincial administration.

ART. 16. In order to bring into effect preventive and curative measures, communes and provinces may unite according to local conditions and mutual convenience.

**ART. 17.** The sum of L.100,000 is to be put aside annually by the Minister of the Interior, for aid to the communes and for the establishment and support of curative institutions. The same provision is to be made by the Minister of Agriculture for the encouragement and aid of institutions of an economic nature and for the improvement of agrarian methods.

**ART. 18.** In communes declared to be infected by pellagra the Minister of Finance is authorized to have salt distributed gratuitously to the sick poor and to their families in quantity sufficient for their food, as directed by the sanitary officer.

**ART. 19.** The execution of the present law shall be provided for by regulations approved by Royal decree and prepared by the Ministers of the Interior, of Agriculture and of Commerce, with the advice of the Superior Board of Health.

## **APPENDIX II.**

### **REGULATIONS FOR THE EXECUTION OF THE LAW OF JULY 21, 1902.**

**ARTICLE 1.** Whoever possesses or detains Indian corn or its products that are in the condition described under (a) and (b) of Art. 1 of the law must notify the local prefect or syndic immediately, stating (a) the quantity of the corn or its products; (b) the persons to whom it belongs and from whom it was obtained (c) the place in which it is kept; (d) the use to which it is to be put.

**ART. 2.** (Until the permission mentioned in Art. 3 of the law has been obtained, this grain cannot be disposed of in any way. The only exception to this rule is with regard to such portions of the corn as are destined for the food of families, known to be poor and unable to provide themselves with sound corn.)

**ART. 3.** Whoever sells, keeps for sale or distributes in any way bread or food made of wheat flour mixed with Indian corn must inform the public by means of labels written in legible characters and placed in conspicuous places upon the goods.

**ART. 4.** No Indian corn coming from foreign countries can be passed at the port or the frontier, nor allowed to circulate in the kingdom without having been first declared sound in conformity with the following provisions. An exception is made for shipments to foreign countries to which the usual rules for goods in transit shall be applied.

ART. 5. (A list of experts, qualified to test imported corn, to be kept in each province. From the list the prefect appoints an expert for any given test.)

ART. 6. The expert, or experts, appointed by the prefect shall take, in the presence of the interested parties or of the captain of the ship, and with the help of the custom house officials, a number of samples proportionate to the size of the cargo. (Methods of taking samples prescribed.)

ART. 7. The above regulations apply also to goods arriving by land; but the taking of samples may be done in one of the internal custom houses, provided the goods travel in closed and sealed cars. Samples must be taken from each car.

ART. 8. (Prescribes the form of certificate to be made out when the samples are taken.)

ART. 9. (The samples taken must be divided into three equal parts. Two of these are to be placed in sealed glass jars, bearing an identification card signed by the inspector and others present at the inspection. The third sample must be used for the summary inspection.)

ART. 10. If on inspection the goods prove undoubtedly sound and fit for food, the inspector shall at once give a declaration (certificate) to this effect, and he shall consign to the harbour authorities or to the collector of customs samples sealed in the glass jars. These samples must be kept for at least three weeks in a dry place at the disposition of the sanitary authorities.



ART. 11. (If on examination it appears that the corn is manifestly spoiled, the inspector must immediately notify the prefect and, if necessary, the owners. One of the sealed jars must then be sent to the owners; the other to the nearest municipal laboratory or agrarian station, where it must be kept for three months in a dry place. During the few days following the owners may demand that the goods shall be tested at the institution or laboratory to which the samples have been sent. If five days elapse without such demand, the merchandise shall be definitely adjudged unsound.)

ART. 12. In case of uncertainty, Article 11 shall apply, but the inspection must be finished within ten days of the arrival of the samples.

ART. 14. (Within ten days of receiving the notice the owners can appeal against the judgment declaring their goods unfit for food and demand a second inspection in state laboratories or some other laboratory indicated by the Minister of the Interior. The second inspection is final.)

ART. 15. Until the inspection is completed the goods cannot circulate in the kingdom nor be ground nor used in any way for human food. Under Article 14, nevertheless, suspected corn, or such as is declared unfit for food, can be unloaded in warehouses provided that it is kept in separate store-rooms under the custody of custom house officials.

ART. 16. (By admitting the unsoundness of a given cargo, the owners can avoid the expense of a test.)

ART. 17. It being ascertained that the merchandise is immature, not properly dessicated, mouldy, or in any other way spoiled or imperfect, the owner must notify in writing the prefect or sub-prefect of the use to which he intends to put it, and the place to which he intends to have it sent. The authorities having collected the necessary information may authorize the circulation of the merchandise in the kingdom, its being ground and used for purposes other than human food upon the following conditions: Indian corn must be directed to a distillery of spirits or a factory of "fecole" and must travel in sealed trucks which cannot be opened except in the presence of customs or police agents. The "bolletta di spedizione" must be given to the authority that has given the permission. Meal must be denatured in the manner determined upon by ministerial regulations. Indian corn that is to be ground must be sent to mills designated by the authorities. The meal must be denatured according to the regulations. The use of Indian corn for the feeding of animals can only be permitted under guarantees that exclude its use as human food.

ART. 21. (Fines imposed in districts free from pellagra shall be used for the benefit of the districts worst affected.)

ART. 22. The report of each case of pellagra must state, in addition to the notices prescribed by the sanitary regulations, how long the person affected has lived in the commune and whether he has been ill before.

ART. 23. (When several cases of pellagra have appeared in persons previously unaffected who have lived at least a year in the commune the prefect shall apply Article 8 of the law.)

ART. 24. (While observing the forms established by Article 9 of the law, communes may publish special regulations for the prevention and cure of pellagra. The minister of the interior, with the superior board of health, may refuse or annul any regulations contrary to the law or to the general regulations).

ART. 25. The regulations directed by the above article must be applied immediately in communes declared affected with endemic pellagra without prejudice to other measures that may be ordered by the prefect.

ART. 26. In accordance with Article 14 of the law, the inspection of Indian meal, its care and preparation may be delegated to doctors or other persons of recognized capacity or skill. Corn taken to mills, bread shops or confectioners shall be inspected with special vigilance.

ART. 27. In communes declared infected with pellagra where Indian corn known as *quarantina* or *cinqantina* is cultivated the authorities, assisted by the state, must encourage the cultivation of other cereals, potatoes, etc., in its place.

ART. 28. (The use of communal dessicating plants must be gratuitous for all the inhabitants, and if the plant is available cannot be refused under pretext that the grain is the property of persons not belonging to the commune. But in this case compensation

must be made, not only for the cost of the firing, but also for the use of the plant.)

ART. 30. The dessication in public plants of Indian corn that is obviously spoiled or mouldy is not allowed. When such corn belongs to persons notoriously poor it should be, if possible, exchanged for sound corn, in sufficient quantity for the needs of the family. Where there are no institutions for this purpose the exchange must be provided for by the commune.

ART. 31. The list of poor "pellagrosi" shall be compiled and kept up to date by the municipal council (meeting). The list must indicate the name, age, sex and condition of the "pellagrosi" and the families who live with them, and state briefly the provisions made for each "pellagroso."

ART. 32. Curative food shall be administered in periods of each year, each period consisting of not less than 40 days. The maximum term for its administration shall be decided by the communal doctor. The diet must be approved by the "pellagrologic" commission, or by the provincial doctor. Medicines are included in the curative diet.

ART. 33. In order to be given curative food the patient must present a medical certificate, visé by the mayor. The food shall be given in sanitary stations, economic kitchens or similar places, and can be given at the patients' homes only in cases of confinement or advanced pregnancy, or when the doctor in charge certifies that the patient cannot be moved.

ART. 34. The inefficacy or insufficiency of curative

diet, as also the inconvenience of administering it at home, must be certified by the doctor in charge, the medical officer or the sanitary officer. Upon the receipt of such a certificate the syndic shall issue an order of admittance to a "pellagrosario," hospital or other suitable place.

ART. 39. Provincial or communal pellagra commissions shall be constituted upon the decree of the minister of the interior, together with the ministers of agriculture, industry and commerce, upon the demand of the provincial or local councils. The provincial doctor, the professor of hygiene at the university, if there is one, the sanitary inspector and a teacher of an elementary school shall be *ex-officio* members of the commission.

ART. 40. The duties of the commission shall be:

(a) To care for the matters appointed by the law.  
(b) To administer the funds for curative and prophylactic measures against the disease.

(c) To inspect and govern the various institutions.

(d) To call to the attention of the authorities all cases requiring official intervention.

(e) To encourage improved methods in agriculture.

(f) To spread among the school children instruction in regard to pellagra, its causes and remedies.

(g) To compile pellagra statistics.

(h) And to perform such other duties as shall be assigned to them by competent authorities.

ART. 47. (Methods of distributing free salt.) No family shall be given more than 5 kilograms in one

week. [?] The quantity to be given to each individual shall not exceed 8 kg. per annum for adults of 15 years or over, or 5 kg. for children.

Arts. 48, 49. (Punishments for evasion or infringement of provisions of Article 47.)

### APPENDIX III.\*

#### PROCLAMATION OF THE MOST ILLUSTRIOUS AND MOST EXCELLENT PURVEYORS AND SUPERIOR PURVEYORS TO HEALTH.

(Venice 1776.)

The pernicious effects which may result to the health of the poorer inhabitants, and, especially those of the villages of Polesine, Padovano and Veronese, from the wretched food made from immature and spoiled corn (*Sorgbi Turchi*), which has been recovered in great quantities from lands submerged by floods, and damaged by the overflow of rivers in those places, pledge the vigilance and zeal of this Magistrate to prevent, by vigorous measures, the homicidal diseases and epidemics which are accustomed to result from such eventful facts. In consideration also of the report of the most able doctors of medicine of Rovigo, transmitted with recent letters by that Illustrious Representation, the Most Illustrious and Most Excellent Superior Purveyors and Purveyors to Health deem it necessary to make publicly known and understood:

I. That it is intended resolutely to inhibit every one from gathering, or having gathered, from inundated valleys, spoiled corn; and to require those who may have already gathered such corn to report to the Health Office the quantity gathered and the place where it may be stored, in order that all those measures and precautions may be put into effect

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\*From Trattatto Proflattico e Clinico della Pellagra, Lombròso.

which are deemed necessary in the salvation of a good cause, and which are practiced at other similar times.

II. That no one must, either for human food or even for food of animals, make use of corn recovered from water when it has thereby become spoiled and of bad odor: it is also equally forbidden to mix such corn with other sound grain for facilitating its sale, and so having it consumed either by the inhabitants of the villages themselves or their dependencies.

III. In order that every one may be effectively prohibited from bringing to the public markets even a small quantity of said grain, spoiled and of bad odor, with the object of sale or exchange, the Grain Brokers must give notice to the Health Office regarding all corn of this kind which may be found to exist privately or in the public markets, and for this purpose ulterior expedients may be adopted.

IV. It is enjoined, however, as a precise duty of each one of the Health Offices of the said provinces to send one of their Purveyors, along with the Chief Physician and Soldiers, for the inspection of the quality of the grain or meal wherever there may be evidence that the prohibited quality is used; and such grain, if found, shall be put in a place aside, well secured, as well as all similar lots which show such evidence; and notice thereof shall be promptly transmitted to the Magistrate by the respective Illustrious Representatives, where, in conformity with the facts of the examination, he may deliberate upon the destination of said grain or meal as to how



best shall be determined what the serious considerations of the case may demand.

V. Corn of the proscribed quality, when carried to the mills, shall not be ground, and it shall be the duty of all Millers to hold such corn received by them, and to carry all the evidence to that Health Office, which is empowered to act in respect to such evidence.

VI. All Medical Doctors of the City, County and Subject Villages, must transmit weekly to their respective Health Offices, notice of all the sick in whom there shall be doubt as to whether such sickness be due to their feeding on said spoiled grain, indicating the character and symptoms of their illness, for the prompt institution of the necessary measures.

VII. Shopkeepers or Grain Vendors must give notice to the Health Office of any quantity, whatever, of spoiled corn which may be found to have been received by them, and the sale of such grain by them is prohibited under the penalty in force at that time and place, in whatever way the grain may be sold or mixed with other grain of good quality.

VIII. One of the principal duties of the Illustrious Representatives, and of the Health Office, shall, however, be that of preventing the importation or exportation of said spoiled grain, in order that their own territory, or others bordering thereon, may not become involved in the danger of troublesome consequences, and for this purpose they shall give to the Authorities, and the Deputies of the Vil-

lages, orders which they deem most suitable and fitting.

IX. The process of inquisition shall be held publicly, and the judgments delivered secretly, so that aid may be thus secured in the discovery of the transgressors, who shall be severely punished according to the sanitary laws, the Magistrate trusting that from the vigilance and zealous solicitude of the respective Illustrious Representatives and Health Officers he shall receive support in the most efficacious manner for the performance of the essential, prudential measures, whereby may be secured the object contemplated, namely, guaranteeing against menacing disasters, the precious health of so many subjects, too many having already been destroyed by the losses suffered.

These presents ordered printed, published and transmitted in copy to the Most Excellent Podesta and Vice-Captain of Padova, and to the Illustrious Captain and Vice-Podesta of Verona, and the Podesta and Captain of Rovigo, whence to be diffused in the cities and territories respectively, as well as to all the Governments subordinate to their jurisdiction, and to the laws of the Health Offices; and published by every Parish Priest of the villages on festal days during the hour of the greatest concourse of people, and republished every first Sunday of each month till they come to universal knowledge for their punctual performance. *Et sic, etc.*

Given by the Most Excellent Magistrate to the Health of Venezia, the 22nd of November, 1776.

**Almoro Pisani, Superior Purveyor.**

**Polo Querini, Superior Purveyor.**

**Marc' Antonio Zustinian, Purveyor.**

**Gerolamo Antonio Valleresso, Purveyor.**

**Gio. Antonio Ruzini, Purveyor.**

**Giuseppe Antonio Gariboldi, Secretary.**

**The 27th day of November, 1776,**

**Published in the customary places.**

*Printed by the Sons of Antonio Pinelli, Ducal Printers.*

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**From the Bibliography of Pellagra of the famous Librarian,  
F. Salveraglio, 1887, Milano.**

## APPENDIX IV.

The following translation is an example of the kind of popular pamphlets which are distributed in Italy for the education of the people in the prophylaxis of pellagra. This one was prepared by Dr. Antonini and issued by the Pellagrologic Commission of the Province of Udine in 1905:

### ADVICE AND RULES FOR AVOIDING PELLAGRA.

SPOILED CORN IS THE CAUSE OF PELLAGRA, and corn readily becomes spoiled, mouldy or poisonous when harvested too early, before it is ripe, and stored in places which are damp or poorly ventilated; it may also be of poor quality when imported from some other place and may contain a large percentage of damaged grains.

\* \* \*

CINQUANTINA is a variety of corn which should be used only for feeding animals.

\* \* \*

SPOILED CORN MAY BE RECOGNIZED by its pale or greenish color, by the shriveled and cracked surface of the grains which are also covered with greenish, bluish or brownish spots, by its musty odor and its bitterish, disgusting taste.

The damaged corn also weighs less than sound corn; and the surface of spoiled grain lacks the shining appearance of the sound article.

KEEP your corn then in places WELL DRIED AND AIRED.

Distrust WHITE CORN because it is more likely to spoil than other kinds.

IMPORTED CORN IS FREQUENTLY DAMAGED.

\* \* \*

Keep watch over your corn while it is being ground in the MILLS of the country.

If you have carried good corn to the mill see to it that you receive meal ground from that corn, and do not allow the miller to substitute meal ground from inferior grain.

\* \* \*

If your corn is GROUND BY A ROLLER MILL (*a cilindro*) the spoiled grains are not likely to be ground into the meal.

\* \* \*

The establishment of a COMMUNAL, CO-OPERATIVE OR INDEPENDENT BAKERY is a great benefit in a section where pellagra is very severe.

The utmost care should be used when one undertakes the PREPARATION AND BAKING OF BREAD AT HOME.

\* \* \*

Instead of SPENDING YOUR MONEY IN WINES AND LIQUORS, buy wheat bread; limit your use of polenta. If you have milk, eggs, cheese, limit the sale of these articles to others, and use at least a part of such products for your own home food.

\* \* \*

REDUCE the cultivation of corn; EXTEND cultivation on your low lands and do not grow corn in mountainous regions or in very moist soils.

Do NOT BE ASHAMED to go to the doctor if you are a pellagrin; and HAVE YOURSELF ENTERED at THE LOCANDA SANITARIA or at the ECONOMIC KITCHEN.

Get cured in time and so avoid the HOSPITAL or the INSANE ASYLUM.

\* \* \*

Remember that the LAW AGAINST PELLAGRA requires a CURATIVE DIET for pellagrins. It is your RIGHT to demand it, and your DUTY to procure it.

\* \* \*

The CLEANLINESS and HEALTHFULNESS of YOUR HOMES are necessary conditions for preventing the moulding of corn which is kept in your houses.

Never keep your corn in BED ROOMS, and see to it that you have proper places for the STORING and SEASONING OF YOUR GRAIN.

KEEP the corn DRY.

\* \* \*

PROFIT BY YOUR INSTRUCTION IN AGRICULTURE, and better your crops.

\* \* \*

EXERT YOURSELVES TO CO-OPERATE WITH OTHERS FOR YOUR OWN SALVATION by acquiring knowledge of, and interest in the application of the LAW AGAINST PELLAGRA.

## APPENDIX V.

### CORN CROP OF COUNTRIES NAMED, 1907.

NORTH AMERICA:	BUSHELS.	BUSHELS.	BUSHELS.
United States.. . . .		2,592,820,000	
Canada:			
Ontario.. . . .	22,949,000		
Quebec.. . . .	1,420,000	24,369,000	
Mexico.. . . .		70,000,000	2,688,689,000
 SOUTH AMERICA:			
Argentina.. . . .		71,768,000	
Chile.. . . .		1,500,000	
Uruguay.. . . .		5,859,000	78,627,000
 EUROPE:			
Austria-Hungary:			
Austria.. . . .	16,599,000		
Hungary proper.. .	155,616,000		
Croatia-Slavonia ..	17,934,000		
Bosnia-Herzegovina .	6,468,000	196,617,000	
Bulgaria.. . . .		12,000,000	
France.. . . .		24,027,000	
Italy.. . . .		88,428,000	
Portugal.. . . .		9,000,000	
Roumania.. . . .		57,576,000	
Russia:			
Russia proper.. .	41,903,000		
Poland.. . . .	1,000		
Northern Caucasia..	8,860,000	50,764,000	
Servia.. . . .		17,691,000	
Spain.. . . .		25,872,000	481,475,000
 AFRICA:			
Algeria.. . . .		402,000	
Cape of Good Hope..		3,550,000	
Egypt.. . . .		35,000,000	
Natal.. . . .		3,300,000	
Sudan (Anglo-Egyptian)		300,000	42,552,000

**AUSTRALASIA :****Australia :**

Queensland.. . . .	3,820,000		
New South Wales	5,945,000		
Victoria.. . . .	727,000		
Western Australia..	1,000	10,493,000	
New Zealand.. . . .		419,000	10,912,000
			<hr/>
Grand total....			3,300,255,000

From the Year Book, U. S. Department of Agriculture, 1908, page 597.

"This statement from the Yearbook of the Department of Agriculture includes practically all corn-producing countries for which either official or trustworthy commercial estimates of production are available. It is well known, however, that the crop is now cultivated in practically all countries where the climate is favorable to its growth and maturation. It is raised in all the States of Central and South America, in all countries of Southern Europe including, besides those named in the Yearbook, Greece and Turkey, in Asia, and probably in all Asiatic countries where climate is adapted to the culture.

"The official reports of the Government of British India return about 6,000,000 acres under maize in that dependency annually, but include no data as to the quantity produced. A statement furnished this Department by the Japanese Director of Statistics gives the area under corn in Japan, in 1906, as 123,076 acres, yield, 3,127,748 bushels. These data, combined with those in the Year Book, comprise practically all statistical information available on the world corn crop."—Statement kindly furnished by



Mr. Victor H. Olmstead, Chief Bureau Statistics,  
Agricultural Department.

PRODUCTION OF CORN IN THE UNITED STATES, 1906, BY  
STATES.

<i>State or Territory.</i>	<i>Bushels.</i>
Maine.. . . .	567,000
New Hampshire.. . . .	1,092,000
Vermont.. . . .	2,499,000
Massachusetts.. . . .	1,818,000
Rhode Island.. . . .	428,000
Connecticut.. . . .	2,395,000
New York.. . . .	24,250,000
New Jersey.. . . .	10,564,000
Pennsylvania.. . . .	57,275,000
Delaware.. . . .	6,240,000
Maryland.. . . .	24,705,000
Virginia.. . . .	50,050,000
West Virginia.. . . .	23,962,000
North Carolina.. . . .	50,166,000
South Carolina.. . . .	29,229,000
Georgia.. . . .	53,750,000
Florida.. . . .	6,584,000
Ohio.. . . .	136,675,000
Indiana.. . . .	137,835,000
Illinois.. . . .	298,620,000
Michigan.. . . .	60,420,000
Wisconsin.. . . .	49,674,000
Minnesota.. . . .	46,835,000
Iowa.. . . .	287,456,000
Missouri.. . . .	203,634,000
North Dakota.. . . .	8,856,000
South Dakota.. . . .	57,677,000
Nebraska.. . . .	205,767,000
Kansas.. . . .	156,200,000
Kentucky.. . . .	84,823,000
Tennessee.. . . .	83,080,000
Alabama.. . . .	44,835,000
Mississippi.. . . .	45,845,000
Louisiana.. . . .	33,898,000
Texas.. . . .	201,848,000
Oklahoma.. . . .	122,239,000
Arkansas.. . . .	54,035,000
Montana.. . . .	94,000
Wyoming.. . . .	84,000
Colorado.. . . .	2,586,000





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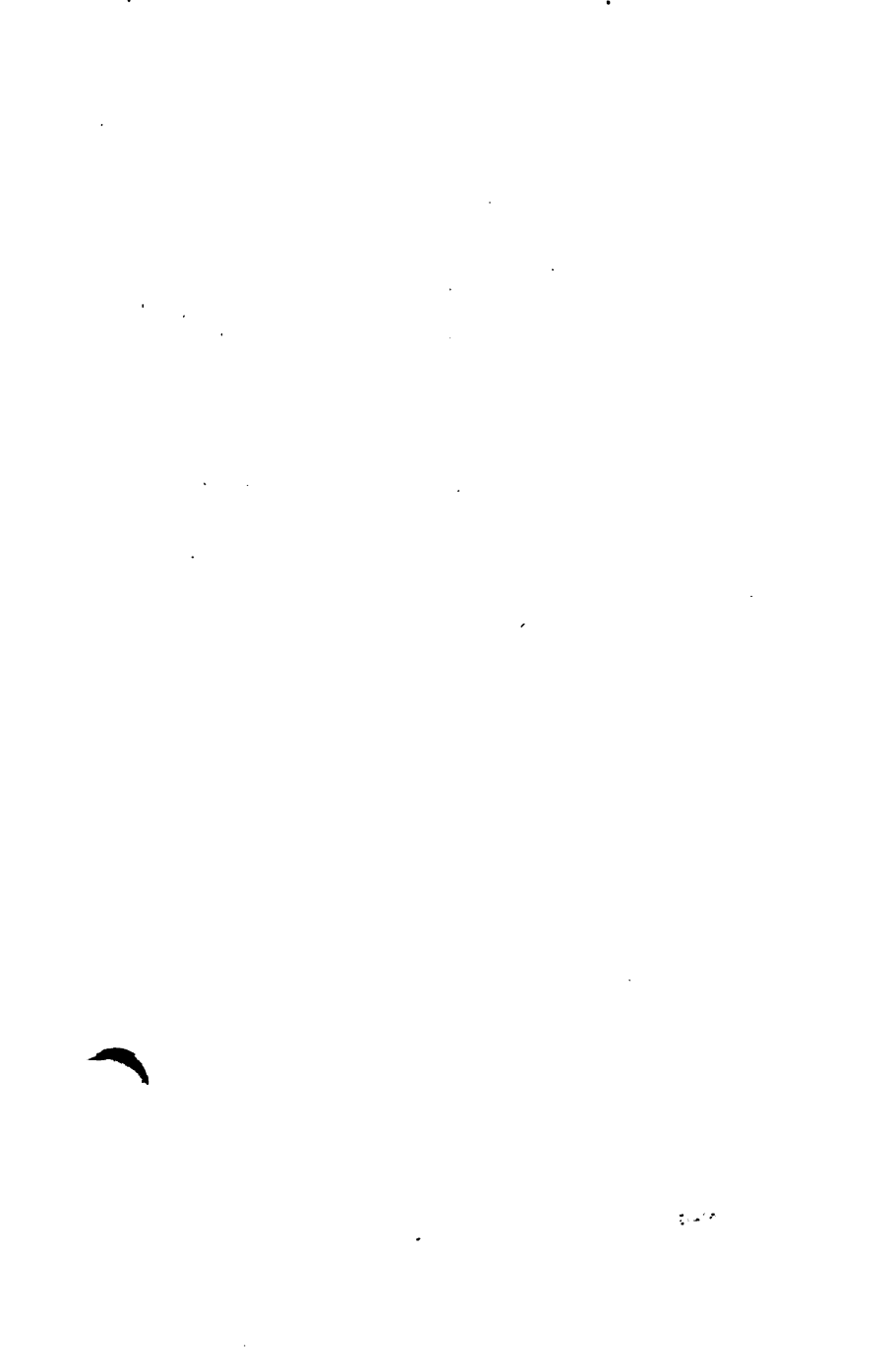
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